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(54) Title: CRYSTAL OF GLUCOKINASE PROTEIN, AND METHOD FOR DRUG DESIGN USING THE CRYSTAL

(54) 発明の名称: グルコキナーゼタンパク質の結晶、及びその結晶を用いたドラッグデザイン方法

(57) Abstract: Glucokinase is crystallized, the three-dimensional structure thereof is analyzed, and then a compound to be bonded to glucokinase is designed on the basis of the coordinate for the resulting three-dimensional structure. Specifically, glucokinase is freed of a part of amino acid residues being on the N-terminal side thereof, to thereby crystallize it, and the three-dimensional structure of the resulting crystal is elucidated through the X-ray crystallographic analysis thereof.

(57) 要約: 本発明は、グルコキナーゼを結晶化し、その三次元構造を解析し、得られる三次元構造座標に基づいて グルコキナーゼに結合する化合物を設計する。 具体的には、グルコキナーゼのN末端側のアミノ酸残基の一部 を欠失させることによってグルコキナーゼを結晶化し、この結晶について×線結晶構造解析によってその三次元構 造を解明することによって達成される。



- 1 -

明細書

グルコキナーゼタンパク質の結晶、及びその結晶を用いたドラッグデザイン方 法

5 技術分野

本発明は、新規なグルコキナーゼタンパク質(以下、「GKタンパク質」ともいう)の結晶、その結晶を用いて得られる三次元構造座標を用いたドラッグデザイン方法などに関する。

10 背景技術

グルコキナーゼ(ATP:D-hexose 6-phosphotran sferaze, EC2.7.1.1)は、哺乳類の4種のヘキソキナーゼアイソザイムのうちの一つ(ヘキソキナーゼIV)である。これらのアイソザイムは同じ反応を触媒するが、グルコースに対する Km 値に差がある。すなわち、

15 ヘキソキナーゼ I、 I I I I O Km 値は 10-6~10-4M であるのに対し、グルコキナーゼともよばれるヘキソキナーゼ I V のグルコースに対する Km 値はずっと大きく、約 10-2M である。ヘキソキナーゼは、解糖系の初期段階に関与する酵素であり、グルコースからグルコース 6 リン酸への反応を触媒する。

グルコキナーゼは、主に肝臓と膵臓ベータ細胞に発現が限局しており、それ 5の細胞におけるグルコース代謝の律速段階を制御することで、体全体の糖代 謝に重要な役割を果たしている。肝臓と膵臓ベータ細胞のグルコキナーゼは、 それぞれスプライシングの違いによりN末端の15アミノ酸の配列が異なって いるが、酵素学的性質は同一である。

10年ほど前から、グルコキナーゼは膵臓ベータ細胞や肝臓のグルコースセンサーとして働くという仮説が提唱されている(Garfinkel D, et al: Am J Physiol 247(3Pt2):R527-536, 1984)。最近のグルコキナーゼ遺伝子操作マウスの結果から、実際にグルコキナーゼは全身のグルコース恒常性に重要な役割を担うことが明らかになっている。

グルコキナーゼ遺伝子を破壊したマウスは、生後まもなく糖尿病で死亡する

(Grupe A, et al: Cell 83:69-78.1995)。一方、グルコキナーゼを過剰発現させたマウスは血糖値が低くなる (Ferre T, et al: Proc Natl Acad Sci U S A 93:7225-7230.1996)。グルコース濃度上昇によってグルコキナーゼ活性が上昇すると、膵臓ベータ細胞と肝細胞の反応は異なるが、いずれも血糖を低下させる方向に作用する。膵臓ベータ細胞は、より多くのインスリンを分泌するようになり、肝臓は糖を取り込みグリコーゲンとして貯蔵すると同時に糖放出を低下させる。

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このようにグルコキナーゼ酵素活性の変動は、肝臓および膵臓ベータ細胞を介した哺乳類のグルコースホメオスタシスにおいて重要な役割を果たしている。 MODY2 (maturity-onset diabetes of the young) と呼ばれる若年に糖尿病を発症する症例においてグルコキナーゼ遺伝子の突然変異が発見され、グルコキナーゼ活性の低下が血糖上昇の原因となっている (Vionnet N, et al: Nature 356:721-722, 1992)。一方グルコキナーゼ活性を上昇させる突然変異をもつ家系も見つかっており、このような人たちは低血糖症状を示す (Glaser B, et al: N Engl J Med 338: 226-230, 1998)。

以上より、グルコキナーゼはヒトにおいてもグルコースセンサーとして働き、グルコース恒常性に重要な役割を果たしている。一方、多くのII型糖尿病患者のグルコキナーゼは変位を受けていないので、グルコキナーゼセンサーシステムを利用した血糖調節は可能と考えられる。グルコキナーゼ活性化物質には膵臓ベータ細胞のインスリン分泌促進作用と肝臓の糖取り込み亢進および糖放出抑制作用が期待できるので、II型糖尿病患者の治療薬として有用と考えられる。

近年、膵臓ベータ細胞型グルコキナーゼが、ラット脳、なかでも特に摂食中 をである視床下部腹内側核(Ventromedial hypothala mus, VMH)に限局して発現していることが明らかにされた。VMHの約 2割の神経細胞は、グルコースレスポンシブニューロンと呼ばれ、従来から体 重コントロールに重要な役割を果たすと考えられてきた。ラットの脳内ヘグルコースを投与すると摂食量が低下するのに対して、グルコース類縁体のグルコ

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サミンの脳内投与によってグルコース代謝を抑制すると過食となる。電気生理学的実験からグルコースレスポンシブニューロンは生理的なグルコース濃度変化(5-20mM)に呼応して活性化されるがグルコサミン等でグルコース代謝を抑制すると活性抑制が認められる。VMHのグルコース濃度感知システムには膵臓ベータ細胞のインスリン分泌と同様なグルコキナーゼを介したメカニズムが想定されている。従って肝臓、膵臓ベータ細胞に加えVHMのグルコキナーゼ活性化を行う物質には血糖是正効果のみならず、多くのII型糖尿病患者で問題となっている肥満をも是正できる可能性がある。

一方、DIABETES, vol. 48, 1698-1705, September 1999 にはヘキソキナー 10 ゼ I からグルコキナーゼの立体構造を予測した旨が記載されているが、実際に 結晶化はされていないし、実用的なものではなかった。

以上より、グルコキナーゼの三次元立体構造を明らかにし、グルコキナーゼ と相互作用する化合物を効率的に見いだすことを可能にすることは、例えば、 糖尿病の治療剤、又は予防剤;網膜症、腎症、神経症、虚血性心疾患、動脈硬 化等の糖尿病の慢性合併症の治療剤、又は予防剤;肥満の治療剤、又は予防剤 の開発に大きな進展をもたらすと考えられる。

現在ではタンパク質の活性中心の解析や反応機作の予測といった作業にコンピュータを利用したCARDD (Computer Aided Rational Drug Design)が実用的なレベルで活用されるようになっている。

20 CARDDによる創薬システムにおいては、ターゲットとなるタンパク質の3次元構造解析データに基づき、タンパク質の活性部位の構造が予測される。そして、その活性部位の構造と結合し得る化合物の候補に関する情報が化合物データベースから取得される。その後、ターゲットとなるタンパク質の活性部位と候補化合物の3次元構造や物理的性質を考慮し、ターゲットとなるタンパク質に結合しうる化合物の候補を選択する。これらの工程が、いわゆるインシリコスクリーニング工程である。

インシリコスクリーニング工程で選択された化合物が、ターゲットとなるタンパク質と結合し、その活性を変化させるかどうかは、実際の試験(ウエット実験)により調べられる。そして、実際にターゲットとなるタンパク質の活性

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を変化させる化合物が医薬の有効成分となる。これにより、実験室で無数の化合物を標的タンパク質に一つ一つ作用させて相互作用を確認するという操作を行うことなく、標的タンパク質と相互作用する化合物を効率よく探し出される。インシリコスクリーニングは、ターゲットとなるタンパク質と結合する化合物の候補を大幅に絞ることができるため医薬品開発に有効な手段であるといえる。

CARDDによる創薬システムにおいては、ターゲットとなるタンパク質の X線構造解析による3次元構造解析データが重要な情報となる。X線構造解析 による3次元構造解析には、解析試料としてターゲットとなるタンパク質の結 10 晶が必要である。したがってCARDDによる創薬システムに基づいてGKに 関連する創薬の開発を進めるためには、GKの結晶が必要である。しかしなが ら、前述のとおりGKは結晶化が困難で、CARDDに必要な情報を与えうる ものではなかった。

15 本発明は、上記従来技術の有する課題に鑑みてなされたものであり、グルコキナーゼの結晶を得ること、及び、当該結晶から得られた情報に基づいてグルコキナーゼに結合する化合物を設計することを目的とする。

発明の開示

- 20 上記目的の少なくともひとつ以上は、以下の発明により解決される。
 - [1] 結晶化に用いることを特徴とする、グルコキナーゼタンパク質。
 - [2] 配列番号5に記載のアミノ酸配列からなることを特徴とする、前記 [1]に記載のタンパク質。
- [3] 配列番号5に記載のアミノ酸配列又はそのアミノ酸配列と実質的に 25 同一のアミノ酸配列からなることを特徴とするタンパク質の結晶。
 - [4] 前記タンパク質がグルコキナーゼタンパク質である、前記[3]に記載の結晶。
 - [5] 配列番号5に記載のアミノ酸配列を有するタンパク質の結晶である、 前記[3]に記載の結晶。

- 5 -

[6] 格子定数が、下記式(1)~(4)

a=b=79.9±4オングストローム … (1)

c=322. 2±15オングストローム … (2)

 $\alpha = \beta = 90^{\circ}$... (3)

5 $\gamma = 120^{\circ}$ ··· (4)

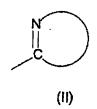
を満たす、前記[3]に記載の結晶。

- [7] 空間群がP6₅22である、前記[6]に記載の結晶。
- [8] 表1に記載の三次元構造座標データによって特定されるタンパク質の結晶。
- 10 [9] 表1に記載の三次元構造座標データの少なくとも一つのデータを変更した三次元構造座標データにおいて、表1に記載の三次元構造座標データで示されるアミノ酸の主鎖の原子(Cα原子)と、該Cα原子と対応する前記変更した三次元構造座標データで示されるCα原子との平均二乗偏差が、0.6 オングストローム以下である結晶。
- [10] 化合物結合部位が、配列番号5に示すアミノ酸配列における、チロシン61~セリン69、グルタミン酸96~グルタミン98、イソロイシン159、メチオニン210~チロシン215、ヒスチジン218~グルタミン酸221、メチオニン235、アルギニン250、ロイシン451~リジン459のアミノ酸残基の少なくともひとつによって構成される、[3]~[9]のいずれかに記載の結晶。
 - [11] 配列番号5に記載のアミノ酸配列又はそのアミノ酸配列と実質的に同一のアミノ酸配列からなるタンパク質と該タンパク質に結合可能な化合物との複合体を含む結晶。
 - [12] 前記化合物が、式(I)で表される、前記[11]に記載の結晶。

$$\begin{array}{c|cccc}
R^1 & & & & & & & \\
R^2 & & & & & & & & \\
R^2 & & & & & & & & \\
NH_2 & & & & & & & \\
\end{array}$$

(i)

[式中、 R^1 は、Nロゲン原子、-S-(O)p-A、-S-(O)q-B又は-O-Bを示し(ここで、p及びqは同一又は異なって、 $0\sim2$ の整数を示し、Aは置換されていてもよい直鎖の C_1-C_6 アルキル基を示し、Bは置換されていてもよい五員環又は六員環のアリール基又はヘテロアリール基を示し、 R^2 は水素原子又はN口ゲン原子を示し、



は、アミド基に結合した炭素原子の隣に窒素原子を有する、置換されていても 10 よい単環の又は双環のヘテロアリール基を示す]

[13] 前記化合物が、式(IIIa) \sim 式(IIIc) で表されるいずれかの化合物である前記[12]に記載の結晶。

(IIIa)

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$$0 = \stackrel{\mathsf{CH}_3}{\underbrace{\mathsf{H}_3}} 0 \qquad 0 \qquad \stackrel{\mathsf{S}}{\underbrace{\mathsf{NH}_2}} \mathsf{CH}_3 \qquad (IIIc)$$

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- [14] 配列番号8に記載のアミノ酸配列からなることを特徴とする、前記 [1] に記載のタンパク質。
- [15] 配列番号8に記載のアミノ酸配列又はそのアミノ酸配列と実質的に同一のアミノ酸配列からなることを特徴とするタンパク質の結晶。
- 10 [16] 前記タンパク質がグルコキナーゼタンパク質である、前記 [15] に記載の結晶。
 - [17] 配列番号8に記載のアミノ酸配列を有するタンパク質の結晶である、 前記[15]に記載の結晶。
 - [18] 格子定数が、下記式
- 15 a=b=103.2±5オングストローム … (5)

c=281.0±7オングストローム … (6)

$$\alpha = \beta = 90^{\circ} \quad \cdots \quad (7)$$

 $\gamma = 120^{\circ}$... (8)

を満たす、前記[15]に記載の結晶。

20 [19] 空間群が P6522 である、前記 [18] に記載の結晶。

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[20] 表2に記載の三次元構造座標データによって特定されるタンパク質の結晶。

[21] 表2に記載の三次元構造座標データの少なくとも一つのデータを変更した三次元構造座標データにおいて、表2に記載の三次元構造座標データで示されるアミノ酸の主鎖の原子($C\alpha$ 原子)と、該 $C\alpha$ 原子と対応する前記変更した三次元構造座標データで示される $C\alpha$ 原子との平均二乗偏差が、0.6オングストローム以下である結晶。

[22] 配列番号2に記載のアミノ酸配列を有するタンパク質のN末端、C 末端のいずれかまたは両方から、1~50個のアミノ酸残基を欠損したアミノ 酸配列を有するタンパク質を製造するタンパク質製造工程と、

前記タンパク質製造工程で得られたタンパク質と結合する化合物と、前記タンパク質製造工程で得られたタンパク質とを反応させるタンパク質反応工程とを含む、

タンパク質及びそのタンパク質と結合する化合物の複合体を含む結晶の製造 15 方法。

[23] タンパク質の結晶を製造する方法であって、

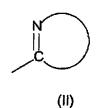
配列番号5に記載のアミノ酸配列又はそのアミノ酸配列と実質的に同一のアミノ酸配列を含みグルコキナーゼ活性を有するタンパク質、及び該タンパク質に結合可能な化合物を用いることを特徴とする、結晶の製造方法。

20 [24] 前記タンパク質に結合可能な化合物が、式(I)で表される化合物 であることを特徴とする、前記[23]に記載のタンパク質の結晶の製造方法。

$$\begin{array}{c|c}
R^1 & O \\
N & C \\
NH_2 & N
\end{array}$$

[式中、 R^1 は、Nロゲン原子、-S-(O)p-A、-S-(O)q-B又は-O-Bを示し(ここで、p及びqは同一又は異なって、 $0\sim2$ の整数を示し、Aは置換されていてもよい直鎖の C_1-C_6 アルキル基を示し、Bは置換されていてもよい五員環又は六員環のアリール基又はヘテロアリール基を示し、

5 R²は水素原子又はハロゲン原子を示し、



は、アミド基に結合した炭素原子の隣に窒素原子を有する、置換されていても よい単環の又は双環のヘテロアリール基を示す)

- 10 [25] 共結晶法又はソーキング法による、前記[23]、又は[24]に 記載の結晶の製造方法。
 - [26] タンパク質の立体構造情報に基づいて該タンパク質に結合する化合物の構造をデザインするドラッグデザイン方法であって、

該タンパク質の立体構造情報が、前記[3]~[13]、又は[15]~[2 15 1]のうちのいずれか一項に記載の結晶を解析することによって得られる情報 であることを特徴とする、ドラッグデザイン方法。

[27] 前記立体構造情報に基づいて、前記タンパク質の化合物結合部位を 推測する結合部位推測工程と、

前記結合部位推測工程で推測された化合物結合部位に適合する化合物を、化合 20 物ライブラリより選択する選択工程と、

を含むことを特徴とする、前記[26]に記載のドラッグデザイン方法。

[28] 前記立体構造情報に基づいて、前記タンパク質の化合物結合部位を 推測する結合部位推測工程と、

前記結合部位推測工程で推測された化合物結合部位に適合する化合物の構造を 25 構築する化合物構造構築工程と、

を含むことを特徴とする、前記[26]に記載のドラッグデザイン方法。

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[29] 前記立体構造情報に基づいて、前記タンパク質の化合物結合部位を 推測する結合部位推測工程と、

前記結合部位推測工程で推測された化合物結合部位と該化合物結合部位に適合 する化合物とが相互作用するように化合物の構造を目視によりデザインするデ ザイン工程と、

を含むことを特徴とする、前記[26]に記載のドラッグデザイン方法。

- [30] 前記化合物結合部位が、配列番号5に示すアミノ酸配列における、 チロシン61~セリン69、グルタミン酸96~グルタミン98、イソロイシ ン159、メチオニン210~チロシン215、ヒスチジン218~グルタミ
- ン酸221、メチオニン235、アルギニン250、ロイシン451~リジン 10 459のアミノ酸残基の少なくともひとつによって構成されている、前記[2 6]~[29]のうちのいずれか一項に記載のドラッグデザイン方法。
- [31] さらに、前記化合物結合部位に適合すると推定される候補化合物の 生理活性を測定する工程を含む、前記 $[26] \sim [30]$ のいずれか一項に記 載のドラッグデザイン方法。 15
 - [32] さらに、前記化合物結合部位に適合すると推定される候補化合物と、 配列番号5に記載のアミノ酸配列又はそのアミノ酸配列と実質的に同一のアミ ノ酸配列を含むタンパク質とを接触させ、その候補化合物が該タンパク質に結 合するか否か判定する結合判定工程を含む、前記[26]~[30]のいずれ か一項に記載のドラッグデザイン方法。
 - [33] 前記[26]~[30]のいずれか一項に記載のドラッグデザイン 方法によって選択された化合物群を化合物アレイとして組み合わせることを含 む化合物アレイの製造方法。

25 図面の簡単な説明

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図1は、グルコキナーゼの三次元構造を示すリボン図である。

(図 1a は、グルコキナーゼ (Δ 1-1 1)/グルコース/化合物 1 (式 IIIaの化合物) の構造を示すリボン図である。また、右図は、左図を回転した図で ある。)

(図1bは、グルコキナーゼ(Δ 1-15)単体の構造を示すリボン図である。 また、右図は、左図を回転した図である。)

図 2 は、グルコキナーゼ (Δ 1-1 1) の結合部位に対する化合物 1 (式 IIIa の化合物) の結合様式を示す図である。

5 図 3 は、グルコキナーゼ (Δ 1-1 1) の結合部位の構造を示す図である。

発明を実施するための最良の形態

本明細書において、アミノ酸、ペプチド、蛋白質は下記に示すIUPAC-IUB生化学命名委員会(CBN)で採用された略号を用いて表される。また、特に明示しない限りペプチド及び蛋白質のアミノ酸残基の配列は、左端から右端にかけてN末端からC末端となるように、またN末端が1番になるように表される。

以下、本発明の各実施態様について詳細に説明する。

15 (グルコキナーゼタンパク質)

10

まず、本発明は、結晶化に用いることを特徴とする、グルコキナーゼタンパク質を提供する。グルコキナーゼタンパク質(GKタンパク質)は、上述のように、生体内で極めて重要な糖の代謝に関与している。したがって、GKタンパク質の三次元構造を明らかにし、GKタンパク質の活性部位を解明することによって、GKタンパク質に結合する化合物(すなわち、活性化剤又は阻害剤)を探索することができる。よって、GKタンパク質の三次元構造を明らかにすることは重要である。

タンパク質の3次元構造を明らかにする手法として、X線結晶構造解析が良く知られている。即ち、タンパク質を結晶化し、その結晶に単色化されたX線25 をあて、得られたX線の回折像をもとに、該タンパク質の3次元構造を解明する(Blundell, T. L. 及びJohnson, L. N., PROTEIN CRYSTALLOGRAPHY, 1-565頁, (1976) Academic Press, New York)。GKタンパク質のX線結晶構造解析に供するために、まず、GKタンパク質を結晶化する必要がある。

ここで、本発明の「GKタンパク質」とは、配列番号2に示すアミノ酸配列を有するヒト由来の肝臓型グルコキナーゼと、配列番号2と実質的に同一のアミノ酸配列を含有するタンパク質をいう。ここで当該実質的に同一のアミノ酸配列を含有するタンパク質としては、グルコキナーゼ活性を有するものが好ましい。したがって、本明細書では、GKタンパク質は、ヒト由来の肝臓型グルコキナーゼのみならず、ヒト由来の膵臓型グルコキナーゼ、マウス、ラット、サル等の非ヒト由来GKタンパク質をも含む。本発明では、ヒト肝臓型グルコキナーゼが好ましく用いられる。ヒト由来のグルコキナーゼにおいて、肝臓型と膵臓型ではN末端の15アミノ酸残基が相違する。ここで、「グルコキナーゼ活性」とは、グルコースからグルコース6リン酸への反応を触媒する活性をいう。

10

タンパク質の結晶化が一般的に困難なことは良く知られており、GKタンパ ク質をそのまま結晶化することはできなかった。本発明者らは、種々、試行錯 誤による実験の結果、GKタンパク質のN末端側のアミノ酸を11個、又は15個を欠失させることによって、始めてGKタンパク質の結晶化に成功した。 15 欠失させた領域は、結晶化を試みた際に球状のGKタンパク質分子より突出し、 その結果、結晶内で隣接するGKタンパク質分子との間で立体的な障害となり GKタンパク質が結晶となるのを妨げていたと考えられる。すなわち、本発明 では、アミノ酸配列が既知でありながら結晶化には成功していなかったグルコ キナーゼにおいて、N末端側の11個のアミノ酸残基を欠失させたGKタンパ 20 ク質(配列番号5)、又はN末端側の15個のアミノ酸残基を欠失させたGK タンパク質(配列番号8)を用いることにより、GKタンパク質の結晶を得た。 ただし、欠失させるアミノ酸は、隣接する結晶との間で立体的な障害がなくな る範囲であればその数は限定されない。具体的には、例えば、配列番号2で表 されるアミノ酸配列において、N末端側の1~50個、好ましくは3~30個、 25 より好ましくは $5\sim25$ 個、さらに好ましくは $8\sim18$ 個、特に好ましくは11~15個のアミノ酸残基を欠失させたアミノ酸配列などが本発明において用 いられる。また、C末端側の $1\sim8$ 個、好ましくは $1\sim7$ 個、より好ましくは $2\sim6$ 個のアミノ酸残基を欠失させたアミノ酸配列などが本発明において用い

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られる。

(グルコキナーゼタンパク質の結晶及びその製造方法)

次に、本発明においては、配列番号5、及び配列番号8に記載のアミノ酸配列又はそのアミノ酸配列と実質的に同一のアミノ酸配列を含むタンパク質を含む結晶を提供する。

上述したように、結晶化に供するGKタンパク質としては、配列番号 5、及び/又は配列番号 8 で表されるアミノ酸配列又はそれと実質的に同一のアミノ酸配列を含むタンパク質などが用いられる。

配列番号5、及び/又は配列番号8で表されるアミノ酸配列又はそれと実質 10 的に同一のアミノ酸配列を含むタンパク質(以下、配列番号2で表されるアミ ノ酸配列又はそれと実質的に同一のアミノ酸配列を有するタンパク質と併せて 「GKタンパク質」と略すこともある)は、結晶化が可能であればよく、その アミノ酸配列は特に制限されない。ここで、配列番号5、及び/又は配列番号 8 に記載のアミノ酸配列と実質的に同一のアミノ酸配列を含むタンパク質は、 15 グルコキナーゼ活性を有している必要はなく、ドラッグデザインに必要な情報 を得ることができる結晶構造を有するものであれば、不活性な変異体(例えば、 ATPの結合部位に変異を有することにより不活性化した変異体)であってもよ い。ここで、配列番号2又は5で表されるアミノ酸配列と実質的に同一のアミ ノ酸配列を含むタンパク質としては、配列番号2又は5で表わされるアミノ酸 20 配列と約60%以上、好ましくは約70%以上、さらに好ましくは約80%以 上、なかでも好ましくは約90%以上、最も好ましくは約95%以上の相同性 を有するアミノ酸配列などが挙げられる。また、配列番号2又は5で表される アミノ酸配列と実質的に同一のアミノ酸配列を含むタンパク質として、例えば、 配列番号 2 又は 5 に記載のアミノ酸配列において $1\sim1$ 0 個、好ましくは $1\sim1$ 25 5個、さらに好ましくは $1\sim3$ 個、さらに好ましくは $1\sim2$ 個のアミノ酸残基

GKタンパク質の3次元構造解析は、例えば、次のようにして行う。まず、 タンパク質を精製する。そして、結晶化、X線回折強度データ収集、各回折斑

が置換、欠失、付加および/または挿入されたアミノ酸配列が例示される。

点の位相決定、電子密度計算、分子モデル作成、構造の精密化などの一連の工程を行う。タンパク質構造解析を行うための主要な設備として、結晶化用インキュベーター、双眼顕微鏡、X線回折計、3次元コンピュータグラフィックス装置などが用いられる。具体的にタンパク質の結晶を作製する実験過程は、タンパク質を大量に(数mg以上が好ましい。)精製する段階、結晶が得られる条件を広く検索する段階、X線解析に適した良質の結晶を得る段階に分けられる。以下、各工程について具体的に説明する。

5

結晶化に際しては、GKタンパク質を、高純度に精製する。精製方法としては、公知のものが利用でき、例えば、カラムクロマトグラフィー、塩析、遠心10 分離などが用いられる。

精製されたGKタンパク質は、結晶化し、X線結晶構造解析のための試料とする。結晶化は、蒸気拡散法や透析法等の公知の方法に基づいて行われる。タンパク質の結晶を得る際に、タンパク質の純度・濃度、温度、pH、使用する沈殿剤濃度等多くの要素を検討する必要がある。結晶化条件の検討は、市販のスクリーニング試薬を使用して広い範囲で行うことができ、1つの条件に1~2%濃度のタンパク質溶液を1~2μLずつ使用して検索することが好ましい。こうして微結晶などが得られた場合には、さらに条件を精密化することが好ましい。

なお、GKタンパク質の結晶を得るためには非常に多くの条件を検索しなけれ 20 ばならない。従って、結晶化条件の検討のためにも、タンパク質の大量発現系 を構築することが好ましい。一般にタンパク質のうち、結晶になるものの多く は、溶液状態で単分散であり、多分散のものは大体において結晶化しない。そ こで、GKタンパク質のN末端を順次切除し、得られたタンパク質について、光 散乱装置を用いてタンパク質溶液の単分散性を判定し、試料が結晶化に適して 25 いるかどうかを検討しても良い。

次に、得られたGKタンパク質の結晶を用いて、X線回折強度測定を行う。 最近では、結晶を細い糸の輪などですくって液体窒素温度に急速冷却してその まま低温で測定する方法も利用されている。回折X線の強度測定は、通常、イ メージングプレートなどの2次元検出器によって行う。X線を当てながら結晶

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を回転させることで発生する多くの回折線をイメージングプレートに記録し、 記録された回折強度をレーザーを当てることにより読み取る。

次に、重原子ソーキング法や共結晶化法により重原子同型置換体を調製することが好ましい。これを使用して多重同型置換法 (MIR法) によりタンパク質 結晶の位相を決定することができる。重原子を導入する代わりに、複雑な波長のX線による回折強度データに基づいて位相を決定する多波長異常散乱法 (MAD法) も利用できる。類似構造を有する分子が既に解析されている場合には、その分子構造を結晶中にあてはめて初期構造を得ることができ、これをもとにフーリエ合成図を描き、残りの部分の構造を解明して全構造を決定する分 子置換法 (MR法) も知られている。

位相が上記の方法で決定したならば、これより電子密度を求める。この精度は、反射の数(分解能)と使用した反射の精度による。分解能は使用する反射の最小面間隔で表す。この電子密度図から分子モデルを組み立てる。分子モデルを組み立てると原子座標が得られるので、これより構造因子の計算値を求め、

15 この大きさを観測値に近づける最小自乗法により原子パラメータの精密化を行う。このようにしてできるだけ妥当な構造情報を取得する。

本発明においては、配列番号 5 に示すG K 9 ンパク質の結晶を調製することに成功している(後述の実施例参照)。そしてこのようにして得られたG K 9 ンパク質の結晶は、格子定数が、下記式(1)~(4):

20 a=b=79.9±4オングストローム … (1) c=322.2±15オングストローム … (2) α=β=90° … (3) γ=120° … (4)

を満たすものであった。また、この結晶は、空間群が $P6_522$ であることが解明された。ここで、前記a=bは 79.9 ± 3 オングストロームであることが好ましく、 79.9 ± 2 オングストロームであることがより好ましく、 79.9 ± 1 オングストロームであることがさらに好ましい。また、前記cは 322.2 ± 10 オングストロームであることが好ましく、 322.2 ± 8 オングストロームであることがより好ましく、 322.2 ± 5 オングストロームであることがさらに好ましい。

- 16 - このようにして得られたGKタンパク質結晶の3次元構造座標を表1に示す。

	表1							
	ATOM	1	CB	THR	14	25. 972 -34. 025	76. 567	1. 00 51. 12
5	MOTA	2	0G1	THR	14	27. 398 -34. 012	76. 715	1.00 51.49
	ATOM	3	CG2	THR	14	25. 626 -34. 173	75. 095	1. 00 49. 96
	ATOM	4	C	THR	14	24. 138 -32. 317	76. 374	1. 00 50. 95
	ATOM	5	0	THR	14	24. 246 -31. 685	75. 330	1. 00 52. 42
	ATOM	6	N	THR	14	25. 108 -32. 861	78. 611	1. 00 51. 41
10	ATOM	7	CA	THR	14	25. 384 -32. 717	77. 154	1. 00 50. 49
	ATOM	8	N	LEU	15	22. 957 -32. 673	76. 871	1. 00 49. 75
	ATOM	9	CA	LEU	15	21. 733 -32. 307	76. 167	1. 00 49. 25
	ATOM	10	CB	LEU	15	20. 496 -32. 824	76. 904	1. 00 52. 56
	ATOM	11	CG	LEU	15	20. 439 -34. 307	77. 291	1. 00 55. 08
15	ATOM	12	CD1	LEU	15	21. 186 -34. 524	78. 610	1. 00 53. 67
	ATOM	13	CD2	LEU	15	18. 980 -34. 742	77. 438	1. 00 54. 84
	ATOM	14	C	LEU	15	21. 676 -30. 781	76. 078	1. 00 48. 68
	ATOM	15	0	LEU	15	21. 397 -30. 208	75. 023	1. 00 47. 52
	ATOM	16	N	VAL		21. 955 -30. 128	77. 201	1. 00 47. 07
20	ATOM	17	CA	VAL		21. 950 -28. 677	77. 265	1. 00 44. 96
	ATOM	18	CB	VAL		21. 988 -28. 188	78. 733	1. 00 46. 09
	ATOM	19		VAL		22. 239 -26. 684	78. 784	1. 00 44. 09
	ATOM	20		VAL		20. 670 -28. 523	79. 418	1. 00 45. 38
	ATOM	21	C	VAL		23. 142 -28. 097	76. 512	1. 00 43. 58
25	ATOM	22	0	VAL		23. 004 -27. 110	75. 790	1. 00 41. 54
	ATOM	23	N	GLU		24. 310 -28. 712	76. 672	1. 00 43. 48
	ATOM	24	CA	GLU		25. 507 -28. 223	75. 998	1. 00 45. 62
	ATOM	25	CB	GLU		26. 759 -28. 931	76. 532	1. 00 46. 30
	ATOM	26	CG	GLU	17	27. 140 -28. 571	77. 984	1. 00 49. 19

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							11	-	
	ATOM	27	CD	GLU	17	27. 467	-27. 087	78. 191	1. 00 50. 74
	ATOM	28	0E1	GLU	17	28. 238	-26. 520	77. 386	1. 00 50. 39
	MOTA	29	0E2	GLU	17	26. 966	-26. 488	79. 170	1. 00 50. 85
	ATOM	30	C	GLU	17	25. 417	-28. 378	74. 479	1. 00 45. 93
5	ATOM	31	0	GLU	17	26. 097	-27. 666	73. 735	1. 00 44. 10
	MOTA	32	N	GLN	18	24. 577	-29. 303	74. 020	1. 00 45. 41
	MOTA	33	CA	GLN	18	24. 400	-29. 513	72. 588	1. 00 46. 37
	MOTA	34	CB	GLN	18	23. 643	-30. 818	72. 307	1. 00 49. 99
	ATOM	35	CG	GLN	18	24. 488	-32. 086	72. 423	1. 00 55. 59
10	ATOM	36	CD	GLN	18	23. 701	-33. 352	72. 088	1. 00 58. 40
	ATOM	37	0E1	GLN	18	23. 158	-33. 489	70. 988	1. 00 60. 78
	ATOM	38	NE2	GLN	18	23. 638	-34. 280	73. 037	1. 00 56. 40
	ATOM	39	С	GLN	18	23. 617	-28. 338	72. 014	1. 00 44. 35
	MOTA	40	0	GLN	18	23. 849	-27. 912	70. 885	1. 00 43. 20
15	ATOM	41	N	ILE	19	22. 677	-27. 821	72. 791	1. 00 41. 97
	ATOM	42	CA	ILE	19	21. 895	-26. 689	72. 327	1. 00 40. 37
	ATOM	43	CB	ILE	19	20. 631	-26. 500	73. 193	1. 00 39. 71
	ATOM	44	CG2	ILE	19	19. 976	-25. 166	72. 894	1. 00 39. 42
	ATOM	45	CG1	ILE	19	19. 653	-27. 653	72. 915	1. 00 40. 83
20	ATOM	46	CD1	ILE	19	18. 356	-27. 599	73. 719	1. 00 38. 38
	MOTA	47	C	ILE	19	22. 764	-25. 431	72. 344	1. 00 39. 01
	MOTA	48	0	ILE	19	22. 746	-24. 644	71. 394	1. 00 40. 12
	ATOM	49	N	LEU	20	23. 550	-25. 267	73. 404	1. 00 35. 38
	ATOM	50	CA	LEU	20	24. 423	-24. 109	73. 537	1. 00 34. 35
25	MOTA	51	CB	LEU	20	25. 026	-24. 050	74. 944	1. 00 32. 09
	ATOM	52	CG	LEU	20	24. 050	-23. 887	76. 106	1. 00 30. 92
	ATOM	53	CD1	LEU	20	24. 813	-23. 722	77. 420	1. 00 27. 61
	MOTA	54	CD2	LEU	20	23. 171	-22. 689	75. 843	1. 00 29. 31
	ATOM	55	С	LEU	20	25. 555	-24. 135	72. 518	1. 00 34. 62

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	ATOM	56	0	LEU 20	26. 066 -23. 087	72. 112	1. 00 34. 19
	ATOM	57	N	ALA 21	25. 946 -25. 336	72. 116	1. 00 33. 16
	ATOM	58	CA	ALA 21	27. 030 -25. 509	71. 163	1. 00 34. 30
	ATOM	59	CB	ALA 21	27. 344 -26. 992	70. 993	1. 00 34. 49
5	ATOM	60	C	ALA 21	26. 696 -24. 886	69. 814	1. 00 35. 20
	ATOM	61	0	ALA 21	27. 587 -24. 619	69. 007	1. 00 35. 57
	ATOM	62	N	GLU 22	25. 412 -24. 652	69. 578	1. 00 36. 75
	ATOM	63	CA	GLU 22	24. 961 -24. 053	68. 329	1. 00 37. 80
	ATOM	64	CB	GLU 22	23. 435 -24. 102	68. 256	1. 00 41. 47
10	ATOM	65	CG	GLU 22	22. 878 -23. 851	66. 867	1. 00 47. 91
	ATOM	66	CD	GLU 22	21. 384 -24. 128	66. 767	1. 00 49. 95
	ATOM	67	0E1	GLU 22	20. 857 -24. 163	65. 630	1. 00 50. 84
	ATOM	68	0E2	GLU 22	20. 741 -24. 307	67. 822	1. 00 50. 26
	ATOM	69	C	GLU 22	25. 444 -22. 605	68. 177	1. 00 37. 38
15	ATOM	70	0	GLU 22	25. 380 -22. 039	67. 088	1. 00 38. 34
	ATOM	71	N	PHE 23	25. 928 -22. 012	69. 268	1. 00 35. 41
	ATOM	72	CA	PHE 23	26. 426 -20. 636	69. 249	1. 00 33. 38
	ATOM	73	CB	PHE 23	26. 224 -19. 962	70. 614	1. 00 31. 59
	ATOM	74	CG	PHE 23	24. 826 -19. 470	70. 843	1. 00 29. 81
20	ATOM	75		PHE 23	23. 836 -20. 328	71. 310	1. 00 26. 48
	ATOM	76	CD2	PHE 23	24. 489 -18. 151	70. 555	1. 00 28. 79
	ATOM	77		PHE 23	22. 520 -19. 882	71. 487	1. 00 29. 30
	ATOM	78		PHE 23	23. 177 -17. 691	70. 727	1. 00 31. 65
	ATOM	79	CZ	PHE 23	22. 189 -18. 563	71. 195	1. 00 28. 91
25	ATOM	80	С	PHE 23	27. 899 -20. 542	68. 877	1. 00 33. 33
	ATOM	81		PHE 23	28. 396 -19. 467	68. 549	1. 00 34. 12
	ATOM	82	N	GLN 24	28. 596 -21. 670	68. 940	1. 00 32. 75
	ATOM	83		GLN 24	30. 016 -21. 716	68. 620	1. 00 32. 56
	ATOM	84	CB	GLN 24	30. 543 -23. 147	68. 778	1. 00 35. 53

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	ATOM	85	CG	GLN 24	30. 817 -23. 603	70. 210	1. 00 37. 84
	ATOM	86	CD	GLN 24	31. 214 -25. 074	70. 266	1. 00 42. 36
	ATOM	87	0E1	GLN 24	31. 802 -25. 601	69. 320	1. 00 43. 06
	ATOM	88	NE2	GLN 24	30. 902 -25. 739	71. 375	1. 00 40. 61
5	ATOM	89	C	GLN 24	30. 335 -21. 233	67. 208	1. 00 31. 93
	ATOM	90	0	GLN 24	29. 508 -21. 320	66. 299	1. 00 30. 32
	ATOM	91	N	LEU 25	31. 548 -20. 717	67. 043	1. 00 31. 64
	ATOM	92	CA	LEU 25	32. 029 -20. 257	65. 751	1. 00 31. 85
	ATOM	93	CB	LEU 25	31. 876 -18. 742	65. 615	1. 00 31. 24
10	ATOM	94	CG	LEU 25	30. 441 -18. 211	65. 563	1. 00 29. 93
	ATOM	95	CD1	LEU 25	30. 436 -16. 690	65. 710	1. 00 28. 63
	ATOM	96	CD2	LEU 25	29. 801 -18. 640	64. 262	1. 00 27. 61
	ATOM	97	C	LEU 25	33. 502 -20. 635	65. 667	1. 00 33. 30
	ATOM	98	0	LEU 25	34. 298 -20. 218	66. 502	1. 00 33. 97
15	ATOM	99	N	GLN 26	33. 856 -21. 450	64. 679	1. 00 34. 57
	ATOM	100	CA	GLN 26	35. 244 -21. 860	64. 496	1. 00 36. 87
	ATOM	101	CB	GLN 26	35. 330 -23. 053	63. 540	1. 00 40. 20
	ATOM		CG	GLN 26	35. 105 -24. 414	64. 182	1. 00 46. 34
	ATOM		CD	GLN 26	33. 863 -24. 462	65. 041	1. 00 48. 48
20	ATOM			GLN 26	33. 918 -24. 229	66. 253	1. 00 49. 27
	ATOM			GLN 26	32. 725 -24. 757	64. 417	
	ATOM			GLN 26	36. 024 -20. 688		
	ATOM			GLN 26		63. 403	1. 00 35. 76
	ATOM			GLU 27		63. 981	1. 00 35. 17
25	ATOM			GLU 27		63. 441	1. 00 37. 77
	ATOM			GLU 27		63. 627	1. 00 40. 11
	ATOM			GLU 27		62. 831	1. 00 47. 14
	ATOM				41. 754 -18. 639	63. 662	1. 00 52. 56
	ATOM	113	0E1	GLU 27	41. 507 -17. 808	64. 567	1. 00 54. 72

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	ATON	114	0E2	2 GLU 27	42. 906 -19. 067	63. 415	1. 00 54. 43
	ATON	I 115	C	GLU 27	37. 878 -19. 511	61. 961	1. 00 37. 80
	ATON	1 116	0	GLU 27	37. 915 -18. 392	61. 446	1. 00 37. 09
	ATON	1 117	N	GLU 28	37. 557 -20. 605	61. 282	1. 00 36. 94
5	ATON	118	CA	GLU 28	37. 261 -20. 535	59. 862	1. 00 36. 18
	ATOM	1119	CB	GLU 28	37. 175 -21. 939	59. 267	1. 00 37. 83
	ATOM	120	CG	GLU 28	37. 826 -22. 039	57. 902	1. 00 41. 72
	ATOM	121	CD	GLU 28	39. 154 -21. 287	57. 843	1. 00 44. 57
	ATOM	122	0E1	GLU 28	40. 033 -21. 531	58. 706	1. 00 46. 91
10	ATOM	123	0E2	GLU 28	39. 313 -20. 446	56. 933	1. 00 44. 10
	ATOM	124	C	GLU 28	35. 973 -19. 779	59. 588	1. 00 34. 66
	ATOM	125	0	GLU 28	35. 860 -19. 089	58. 575	1. 00 33. 91
	ATOM	126	N	ASP 29	34. 994 -19. 926	60. 472	1. 00 32. 44
	ATOM	127	CA	ASP 29	33. 738 -19. 219	60. 301	1. 00 32. 41
15		128			32. 713 -19. 625		
	MOTA				32. 302 -21. 091		
	ATOM				32. 012 -21. 580	60. 173	1. 00 34. 03
	ATOM			ASP 29			
	ATOM		С	ASP 29			
20	ATOM				33. 542 -16. 895		
	ATOM				34. 912 -17. 403		
					35. 274 -16. 016		1. 00 28. 38
	ATOM		CB	LEU 30	36. 101 -15. 901		1. 00 23. 67
25	ATOM			LEU 30	35. 435 -16. 298	64. 289	1. 00 23. 54
25	ATOM			LEU 30	36. 314 -15. 823	65. 433	1. 00 22. 55
	ATOM			LEU 30	34. 038 -15. 674	64. 418	1. 00 24. 55
	ATOM			LEU 30	36. 032 -15. 390	60. 499	1. 00 29. 80
	ATOM			LEU 30	35. 775 -14. 242	60. 139	1. 00 29. 56
	ATOM	142	N	LYS 31	36. 963 -16. 131	59. 906	1. 00 29. 13

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	ATOM 143	CA	LYS 31	37. 704 -15. 609	58. 770	1. 00 30. 46
	ATOM 144	CB	LYS 31	38. 823 -16. 574	58. 365	1. 00 32. 24
	ATOM 145	CG	LYS 31	39. 970 -16. 653	59. 374	1. 00 36. 80
	ATOM 146	CD	LYS 31	41. 091 -17. 577	58. 885	1. 00 40. 49
. 5	ATOM 147	CE	LYS 31	42. 291 -17. 534	59. 829	1. 00 44. 52
	ATOM 148	NZ	LYS 31	43. 443 -18. 369	59. 363	1. 00 47. 22
	ATOM 149	C	LYS 31	36. 746 -15. 391	57. 599	1. 00 31. 28
	ATOM 150	0	LYS 31	36. 918 -14. 464	56. 816	1. 00 32. 79
	ATOM 151	N	LYS 32	35. 730 -16. 243	57. 486	1. 00 30. 96
10	ATOM 152	CA	LYS 32	34. 758 -16. 116	56. 406	1. 00 32. 66
	ATOM 153	CB	LYS 32	33. 868 -17. 364	56. 324	1. 00 32. 27
	ATOM 154	CG	LYS 32	32. 921 -17. 362	55. 135	1. 00 34. 72
	ATOM 155	CD	LYS 32	32. 203 -18. 701	54. 965	1. 00 39. 55
	ATOM 156	CE	LYS 32	31. 272 -18. 678	53. 745	1. 00 42. 65
15	ATOM 157	NZ	LYS 32	30. 699 -20. 026	53. 417	1. 00 42. 72
	ATOM 158	C	LYS 32	33. 890 -14. 868	56. 609	1. 00 32. 63
	ATOM 159	0	LYS 32	33. 607 -14. 140	55. 652	1. 00 32. 25
	ATOM 160	N	VAL 33	33. 463 -14. 629	57. 847	1. 00 30. 17
	ATOM 161	CA	VAL 33	32. 654 -13. 451	58. 149	1. 00 29. 03
20	ATOM 162	CB	VAL 33	32. 154 -13. 460	59. 626	1. 00 30. 49
	ATOM 163		VAL 33			1. 00 31. 03
	ATOM 164		VAL 33	31. 130 -14. 562		1. 00 32. 03
	ATOM 165	C	VAL 33	33. 538 -12. 226	57. 908	1. 00 26. 62
	ATOM 166	0	VAL 33		57. 338	1. 00 22. 25
25	ATOM 167	N	MET 34		58. 317	1. 00 25. 50
	ATOM 168	CA	MET 34	35. 750 -11. 226	58. 142	1. 00 27. 22
	ATOM 169	CB	MET 34	37. 108 -11. 583	58. 748	1. 00 24. 41
	ATOM 170		MET 34	38. 150 -10. 512		1. 00 26. 32
	ATOM 171	SD	MET 34	39. 793 -11. 040	59. 074	1. 00 32. 95

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	ATOM 172	CE MET 34	40. 162 -12. 313	57. 821	1. 00 30. 64
	ATOM 173	C MET 34	35. 927 -10. 879	56. 665	1. 00 29. 30
	ATOM 174	0 MET 34	35. 850 -9. 717	56. 286	1. 00 29. 01
	ATOM 175	N ARG 35	36. 164 -11. 883	55. 827	1. 00 30. 96
5	ATOM 176	CA ARG 35	36. 340 -11. 621	54. 403	1. 00 32. 99
	ATOM 177	CB ARG 35	36. 664 -12. 913	53. 641	1. 00 34. 85
	ATOM 178	CG ARG 35	37. 948 -13. 585	54. 081	1. 00 38. 82
	ATOM 179	CD ARG 35	38. 377 -14. 682	53. 126	1. 00 43. 22
	ATOM 180	NE ARG 35	38. 963 -15. 791	53. 869	1. 00 47. 35
10	ATOM 181	CZ ARG 35	38. 260 -16. 801	54. 366	1. 00 47. 12
	ATOM 182	NH1 ARG 35	36. 946 -16. 850	54. 186	1. 00 48. 27
	ATOM 183	NH2 ARG 35	38. 868 -17. 746	55. 064	1. 00 50. 91
	ATOM 184	C ARG 35	35. 090 -10. 997	53. 797	1. 00 33. 31
	ATOM 185	0 ARG 35	35. 178 -10. 089	52. 966	1. 00 33. 49
15	ATOM 186	N ARG 36	33. 926 -11. 493	54. 206	1. 00 32. 00
	ATOM 187	CA ARG 36	32. 673 -10. 982	53. 675	1. 00 31. 76
	ATOM 188	CB ARG 36	31. 511 -11. 857	54. 158	1. 00 29. 95
	ATOM 189	CG ARG 36	30. 191 -11. 607	53. 441	1. 00 31. 90
	ATOM 190	CD ARG 36	30. 386 -11. 434	51. 929	1. 00 33. 67
20	ATOM 191	NE ARG 36	29. 114 -11. 263	51. 230	1. 00 38. 02
	ATOM 192	CZ ARG 36	28. 229 -12. 238	51.018	1. 00 40. 67
	ATOM 193	NH1 ARG 36	28. 477 -13. 471		1. 00 40. 50
	ATOM 194		27. 087 -11. 979	50. 382	1. 00 41. 02
		C ARG 36		54. 060	1. 00 31. 54
25	ATOM 196	0 ARG 36	31. 959 -8. 718	53. 260	1. 00 30. 75
	ATOM 197	N MET 37	32. 856 -9. 147	55. 276	1. 00 30. 98
	ATOM 198	CA MET 37	32. 720 -7. 774	55. 742	1. 00 30. 21
	ATOM 199	CB MET 37	33. 134 -7. 663	57. 208	1. 00 27. 60
	ATOM 200	CG MET 37	33. 102 -6. 240	57. 761	1. 00 27. 98

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					20		
	ATOM 2	01 SD	MET 37	31. 418	-5. 613	57. 981	1. 00 30. 18
	ATOM 2	02 CE	MET 37	31. 115	-6. 153	59. 683	1. 00 28. 30
	ATOM 2	03 C	MET 37	33. 598	-6. 852	54. 892	1. 00 30. 32
	ATOM 2	04 0	MET 37	33. 162	-5. 782	54. 479	1. 00 31. 66
5	ATOM 2	05 N	GLN 38	34. 835	-7. 272	54. 642	1. 00 30. 60
	ATOM 2	06 CA	GLN 38	35. 774	-6. 500	53. 829	1. 00 31. 68
	ATOM 2	07 CB	GLN 38	37. 126	-7. 206	53. 750	1. 00 32. 18
	ATOM 2	08 CG	GLN 38	38. 051	-6. 918	54. 898	1. 00 36. 36
	ATOM 2	09 CD	GLN 38	39. 318	-7. 743	54. 831	1. 00 37. 65
10	ATOM 2	10 OE	GLN 38	39. 352	-8. 890	55. 275	1. 00 41. 25
	ATOM 2	11 NE2	C GLN 38	40. 362	-7. 170	54. 258	1. 00 39. 99
	ATOM 2	12 C	GLN 38	35. 241	-6. 337	52. 419	1. 00 32. 20
	ATOM 2	13 0	GLN 38	35. 471	-5. 318	51.769	1. 00 32. 83
	ATOM 21	14 N	LYS 39	34. 541	-7. 360	51. 947	1. 00 31. 94
15	ATOM 21	5 CA	LYS 39	33. 965	-7. 343	50. 611	1. 00 33. 33
	ATOM 21	6 CB	LYS 39	33. 515	-8. 754	50. 220	1. 00 34. 32
	ATOM 21		LYS 39		-9. 105	48. 756	1. 00 41. 05
	ATOM 21		LYS 39	32. 994	-8. 183	47. 799	1. 00 43. 55
	ATOM 21		LYS 39		-8. 502	46. 336	1. 00 47. 30
20	ATOM 22		LYS 39				1. 00 48. 42
	ATOM 22						1. 00 32. 37
				32. 578	-5. 676	49. 564	1. 00 33. 02
	ATOM 22		GLU 40	31. 975	-6. 342	51. 613	1. 00 31. 82
	ATOM 22		GLU 40	30. 831	-5. 442	51. 632	1. 00 33. 50
25	ATOM 22		GLU 40	29. 845	-5. 831	52. 737	1. 00 34. 39
	ATOM 22		GLU 40	29. 159	-7. 167	52. 507	1. 00 36. 32
	ATOM 22		GLU 40	28. 562	-7. 293	51. 112	1. 00 38. 53
	ATOM 22		GLU 40	27. 878	-6. 350	50. 660	1. 00 39. 61
	ATOM 22	9 OE2	GLU 40	28. 770	-8. 342	50. 469	1. 00 38. 22

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- 24 -ATOM 230 C **GLU 40** 31. 309 -4.00951. 833 1. 00 33. 20 ATOM 231 **GLU 40** 0 30. 691 -3.07251. 345 1. 00 33. 12 ATOM 232 N MET 41 32. 409 -3.84452. 556 1. 00 33. 18 ATOM 233 CA MET 41 32. 957 -2.51552. 783 1. 00 34. 90 ATOM 234 CB MET 41 34. 173 -2.58553. 706 1. 00 32. 91 MET 41 CG 33. 838 -2.92755. 154 1. 00 34. 83 MET 41 SD 35. 327 -2.98756. 170 1.00 34.41 CE MET 41 35. 747 -1.21656. 267 1.00 36.69 С MET 41 33. 368 -1.94151. 430 1. 00 36. 56 MET 41 0 33. 058 -0.79251. 108 1. 00 34. 98 N ASP 42 34. 054 -2.75850.639 1. 00 36. 46 CA ASP 42 34. 508 -2.34649. 317 1. 00 38. 91 CB ASP 42 35. 318 -3.47048. 674 1. 00 42. 09 CG ASP 42 36. 130 -2.99947. 490 1.00 43.40 OD1 ASP 42 37. 081 -2.21647. 705 1. 00 45. 67 OD2 ASP 42 35.817 -3.41146.350 1. 00 42. 51 ASP 42 C 33. 311 -1. 990 48. 433 1. 00 38. 61 0 ASP 42 33. 366 -1.03647.656 1. 00 39. 03 N ARG 43 32. 232 -2.76148.559 1.00 36.74

ATOM 235 ATOM 236 ATOM 237 ATOM 238 ATOM 239 10 ATOM 240 ATOM 241 ATOM 242 ATOM 243 ATOM 244 15 ATOM 245 ATOM 246 ATOM 247 ATOM 248 ATOM 249 20 CA ARG 43 31.012 -2.52447.788 1.00 33.90 ATOM 250 ARG 43 CB 30. 037 -3. 688 47. 967 1.00 33.80 ATOM 251 ARG 43 CG 30. 324 -4.89047.080 1. 00 34. 68 ATOM 252 CDARG 43 29. 654 -6.16347.614 1.00 34.89 ATOM 253 NE ARG 43 28. 232 -5.99747. 906 1. 00 35. 11 25 ATOM 254 CZ ARG 43 27. 296 -5.72946. 998 1. 00 37. 42 ATOM 255 NH1 ARG 43 27. 620 -5. 589 45. 719 1. 00 39. 98 ATOM 256 NH2 ARG 43 26. 028 -5. 615 47. 366 1. 00 36. 46 ATOM 257 С ARG 43 30. 313 -1.22948. 193 1. 00 34. 64 ATOM 258 ARG 43 0 29. 712 -0.55047. 357 1. 00 35. 89

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	ATOM 259	N GLY 44	30. 382	-0. 892	49. 475	1. 00 31. 21
	ATOM 260	CA GLY 44	29. 744	0. 318	49. 940	1. 00 31. 87
	ATOM 261	C GLY 44	30. 463	1. 579	49. 490	1. 00 33. 29
	ATOM 262	0 GLY 44	29. 854	2. 645	49. 397	1. 00 31. 49
5	ATOM 263	N LEU 45	31. 756	1. 455	49. 200	1. 00 31. 44
	ATOM 264	CA LEU 45	32. 563	2. 595	48. 778	1. 00 32. 24
	ATOM 265	CB LEU 45	34. 033	2. 358	49. 129	1. 00 27. 43
	ATOM 266	CG LEU 45	34. 415	2. 487	50. 601	1. 00 29. 59
	ATOM 267	CD1 LEU 45	35. 832	1. 992	50. 827	1. 00 30. 31
10	ATOM 268	CD2 LEU 45	34. 281	3. 941	51.022	1. 00 30. 45
	ATOM 269	C LEU 45	32. 455	2. 933	47. 294	1. 00 33. 00
	ATOM 270	0 LEU 45	32. 537	4. 098	46. 924	1. 00 32. 78
		N ARG 46	32. 277	1. 911	46. 460	1. 00 34. 18
	ATOM 272	CA ARG 46	32. 179	2. 074	45. 009	1. 00 34. 76
15	ATOM 273	CB ARG 46	32. 320	0. 714	44. 312	1. 00 36. 33
				-0. 119	44. 756	1. 00 39. 02
		CD ARG 46				1. 00 43. 71
	ATOM 276					1. 00 48. 60
		CZ ARG 46				1. 00 49. 59
20		NH1 ARG 46				
		NH2 ARG 46				
		C ARG 46				1. 00 34. 95
	ATOM 281	0 ARG 46				1. 00 32. 49
0=		N LEU 47				
25		CA LEU 47				1. 00 34. 40
	ATOM 284	CB LEU 47			42. 049	
	ATOM 285	CG LEU 47				1. 00 33. 85
		CD1 LEU 47				
	ATOM 287	CD2 LEU 47	29. 381	6. 741	40. 144	1. 00 31. 08

- 26 -ATOM 288 С LEU 47 28. 727 3. 316 42. 625 1. 00 34. 52 ATOM 289 0 LEU 47 27. 535 3. 411 42. 922 1. 00 32. 39 ATOM 290 N **GLU 48** 29. 202 2. 353 41. 841 1.00 34.67 ATOM 291 CA GLU 48 28. 301 1. 378 41. 242 1. 00 36. 59 5 ATOM 292 CBGLU 48 29.010 0.589 40. 134 1. 00 38. 07 ATOM 293 CG**GLU 48** 30. 205 -0. 248 40. 562 1.00 39.26 ATOM 294 CD GLU 48 31. 499 0. 534 40. 580 1.00 40.85 ATOM 295 0E1 GLU 48 32. 571 -0. 106 40. 497 1.00 44.46 ATOM 296 0E2 GLU 48 31. 454 1. 779 40. 682 1. 00 38. 21 10 ATOM 297 C **GLU 48** 27. 600 0.406 42. 188 1.00 37.46 ATOM 298 0 GLU 48 26. 654 -0.26841.778 1. 00 37. 82 ATOM 299 N THR 49 28. 037 0. 321 43. 441 1. 00 36. 85 ATOM 300 CA THR 49 27. 371 -0.59144. 370 1. 00 36. 40 ATOM 301 THR 49 CB28. 212 -1.85544. 645 1. 00 34. 37 ATOM 302 15 0G1 THR 49 29. 554 -1.48044. 969 1.00 33.33 ATOM 303 CG2 THR 49 28. 215 -2.77043. 437 1. 00 32. 44 ATOM 304 C THR 49 27. 032 0.037 45. 703 1. 00 38. 54 ATOM 305 0 THR 49 26. 536 -0.64746. 599 1. 00 40. 86 ATOM 306 N HIS 50 27. 272 1. 335 45. 842 1. 00 38. 89 20 ATOM 307 CA HIS 50 26. 994 1. 990 1. 00 41. 74 47. 115 ATOM 308 CB HIS 50 27. 548 3. 422 47. 130 1.00 44.04 ATOM 309 CG HIS 50 26.666 4. 426 46. 451 1. 00 46. 35 ATOM 310 CD2 HIS 50 25. 795 5. 331 46. 959 1. 00 48. 65 ATOM 311 ND1 HIS 50 26.607 4. 565 45.081 1. 00 47. 18 ATOM 312 25 CE1 HIS 50 25. 738 5. 512 44. 772 1. 00 48. 13 ATOM 313 NE2 HIS 50 25. 231 5. 993 45. 894 1.00 49.20 ATOM 314 C HIS 50 25. 512 2. 030 47. 466 1. 00 42. 66 ATOM 315 0 HIS 50 25. 153 2. 046 48.642 1.00 42.85 ATOM 316 GLU 51 24. 657 2.034 46. 447 1. 00 43. 12

- 27 -ATOM 317 CA GLU 51 23. 213 2. 120 46. 645 1. 00 44. 07 ATOM 318 CB GLU 51 22.555 2. 574 45. 329 1. 00 44. 83 ATOM 319 CG GLU 51 21.051 2.824 45. 399 1. 00 46. 43 ATOM 320 CDGLU 51 20.531 3.691 44. 243 1. 00 48. 89 ATOM 321 5 OE1 GLU 51 20.822 3. 385 43.064 1.00 46.31 ATOM 322 0E2 GLU 51 19.821 4. 683 44. 522 1. 00 50. 83 ATOM 323 GLU 51 C 22. 543 0.848 47. 179 1. 00 44. 27 ATOM 324 GLU 51 0 21.630 0.925 48.000 1.00 45.14 ATOM 325 N GLU 52 22.991 -0.31746. 723 1.00 44.47 10 ATOM 326 CA GLU 52 22. 422 -1.58547. 178 1. 00 44. 81 ATOM 327 CBGLU 52 22. 199 -2.52145. 988 1. 00 47. 15 ATOM 328 CG GLU 52 23. 485 -2.92045. 264 1. 00 53. 66 ATOM 329 CD GLU 52 23. 698 -2.16443. 951 1. 00 57. 63 ATOM 330 0E1 GLU 52 23. 646 -0.90943. 953 1. 00 55. 90 15 ATOM 331 0E2 GLU 52 23. 925 -2.83542. 917 1. 00 57. 72 ATOM 332 C GLU 52 23. 313 -2.29748. 206 1. 00 42. 49 ATOM 333 GLU 52 23. 052 -3.44148. 575 1. 00 43. 45 ATOM 334 N ALA 53 24. 362 -1.62648. 666 1. 00 39. 72 ATOM 335 CA ALA 53 25. 285 -2.22449. 628 1. 00 37. 01 ATOM 336 20 CB ALA 53 26. 589 -1.43849. 645 1. 00 35. 23 ATOM 337 C ALA 53 24. 700 -2.29151. 038 1. 00 35. 27 ATOM 338 0 ALA 53 24. 125 -1.32151. 528 1. 00 34. 63 ATOM 339 N SER 54 24. 845 -3.43951.689 1. 00 32. 88 ATOM 340 CA SER 54 24. 339 -3.59453. 052 1. 00 32. 06 ATOM 341 25 CB SER 54 24. 397 -5.06253. 476 1. 00 30. 23 ATOM 342 OG SER 54 25. 694 -5.57653. 261 1. 00 35. 67 ATOM 343 C **SER 54** 25. 188 -2.74153. 990 1.00 28.49 ATOM 344 0 SER 54 24. 682 -2.14754. 934 1. 00 29. 57 ATOM 345 N VAL 55 26. 485 -2.68453. 724 1. 00 28. 44

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	ATOM 346	CA	VAL 5	27. 386	-1. 876	54. 535	1. 00 28. 63
	ATOM 347	CB	VAL 5	28. 737	-2. 594	54. 726	1. 00 27. 89
	ATOM 348	CG1	VAL 5	29. 660	-1. 766	55. 599	1. 00 26. 89
	ATOM 349	CG2	VAL 5	28. 497	-3. 957	55. 365	1. 00 27. 94
5	ATOM 350	C	VAL 58	27. 559	-0. 551	53. 788	1. 00 29. 80
	ATOM 351	0	VAL 58	28. 367	-0. 430	52. 868	1. 00 28. 14
	ATOM 352	N	LYS 56	26. 787	0. 446	54. 205	1. 00 31. 68
	ATOM 353	CA	LYS 56	26. 788	1. 750	53. 550	1. 00 30. 06
	ATOM 354	CB	LYS 56	25. 727	2. 628	54. 203	1. 00 29. 96
10	ATOM 355	CG	LYS 56	24. 312	2. 124	53. 933	1. 00 29. 47
	ATOM 356	CD	LYS 56	23. 279	2. 935	54. 689	1. 00 31. 68
	ATOM 357	CE	LYS 56	23. 417	2. 767	56. 196	1. 00 30. 78
	ATOM 358	NZ	LYS 56	22. 911	1. 428	56. 648	1. 00 36. 66
	ATOM 359	C	LYS 56	28. 087	2. 535	53. 374	1. 00 28. 33
15	ATOM 360	0	LYS 56	28. 222	3. 256	52. 388	1. 00 30. 83
	ATOM 361	N	MET 57	29. 044	2. 410	54. 287	1. 00 25. 97
	ATOM 362	CA	MET 57	30. 299	3. 149	54. 137	1. 00 23. 92
	ATOM 363	CB	MET 57	31. 098	2. 577	52. 964	1. 00 24. 05
•	ATOM 364		MET 57			53. 075	1. 00 27. 54
20	ATOM 365			32. 303			1. 00 26. 48
							1. 00 21. 76
			MET 57	30. 006	4. 643	53. 887	1. 00 26. 44
	ATOM 368		MET 57		5. 237	52. 903	1. 00 24. 39
	ATOM 369		LEU 58		5. 235	54. 803	1. 00 26. 42
25	ATOM 370		LEU 58			54. 713	1. 00 26. 83
	ATOM 371	-	LEU 58		6. 884	55. 677	1. 00 24. 27
	ATOM 372	CG	LEU 58		6. 043	55. 386	1. 00 30. 26
	ATOM 373		LEU 58		6. 250	56. 473	1. 00 28. 51
	ATOM 374	CD2	LEU 58	25. 874	6. 430	54. 016	1. 00 31. 10

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	ATOM	375	C	LEU	58	29. 932	7. 665	54. 965	1. 00 25. 48
	ATOM	376	0	LEU	58	30. 495	7. 742	56. 053	1. 00 25. 30
	ATOM	377	N	PRO	59	30. 242	8. 476	53. 946	1. 00 24. 56
	ATOM	378	CD	PRO	59	29. 764	8. 341	52. 557	1. 00 24. 76
5	ATOM	379	CA	PRO	59	31. 262	9. 528	54. 063	1. 00 26. 48
	ATOM	380	CB	PRO	59	31. 217	10. 196	52. 686	1. 00 26. 76
	ATOM	381	CG	PRO	59	30. 865	9. 036	51. 769	1. 00 26. 41
	ATOM	382	C	PRO	59	30. 820	10. 478	55. 190	1. 00 26. 49
	ATOM	383	0	PRO	59	29. 656	10. 863	55. 239	1. 00 28. 20
10	ATOM	384	N	THR	60	31. 728	10. 845	56. 092	1. 00 27. 28
	ATOM	385	CA	THR	60	31. 372	11. 720	57. 220	1. 00 27. 77
	ATOM	386	CB	THR	60	31. 994	11. 217	58. 544	1. 00 24. 87
	ATOM	387	0G1	THR	60	33. 400	11. 482	58. 536	1. 00 22. 66
	ATOM	388	CG2	THR	60	31. 767	9. 713	58. 726	1. 00 28. 80
15	ATOM	389	C	THR	60	31. 800	13. 196	57. 085	1. 00 30. 72
	ATOM	390	0	THR	60	31. 405	14. 041	57. 897	1. 00 29. 67
	ATOM	391	N	TYR	61	32. 623	13. 485	56. 084	1. 00 30. 13
	ATOM	392	CA	TYR	61	33. 144	14. 824	55. 844	1. 00 33. 87
	ATOM	393	CB	TYR	61	32. 005	15. 837	55. 684	1. 00 32. 96
20	ATOM	394	CG	TYR	61	31. 409	15. 730	54. 298	1. 00 35. 37
	ATOM	395	CD1	TYR	61	32. 084	16. 251	53. 192	1. 00 36. 43
	ATOM	396	CE1	TYR	61	31. 621	16. 036	51. 890	1. 00 34. 05
	ATOM	397	CD2	TYR	61	30. 244	14. 995	54. 068	1. 00 34. 99
	ATOM	398	CE2	TYR	61	29. 778	14. 772	52. 768	1. 00 33. 96
25	ATOM	399	CZ	TYR	61	30. 475	15. 294	51. 689	1. 00 33. 72
	ATOM	400	ОН	TYR	61	30. 039	15. 064	50. 402	1. 00 37. 69
	ATOM	401	C	TYR	61	34. 156	15. 264	56. 890	1. 00 34. 78
	ATOM	402	0	TYR	61	34. 712	16. 357	56. 806	1. 00 34. 09
	ATOM	403	N	VAL	62	34. 407	14. 407	57. 875	1. 00 36. 47

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	ATOM 404	CA	VAL 62	35. 426	14. 713	58. 869	1. 00 37. 40
	ATOM 405	CB	VAL 62	35. 283	13. 825	60. 116	1. 00 37. 42
	ATOM 406						1. 00 32. 97
	ATOM 407	CG2	VAL 62	33. 937	14. 073	60. 774	1. 00 36. 34
5	ATOM 408	C	VAL 62	36. 695	14. 335	58. 104	1. 00 41. 04
	ATOM 409	0	VAL 62	36. 944	13. 153	57. 865	1. 00 40. 85
	ATOM 410	N	ARG 63	37. 475	15. 331	57. 692	1. 00 43. 48
	ATOM 411	CA	ARG 63	38. 682	15. 070	56. 909	1. 00 48. 27
	ATOM 412	CB	ARG 63	38. 843	16. 126	55. 814	1. 00 47. 25
10	ATOM 413	CG	ARG 63	37. 735	16. 112	54. 783	1. 00 49. 66
	ATOM 414	CD	ARG 63	37. 648	17. 447	54.061	1. 00 50. 62
	ATOM 415	NE	ARG 63	36. 482	17. 523	53. 185	1. 00 51. 28
	ATOM 416						1. 00 50. 52
	ATOM 417	NH1	ARG 63	37. 430	16. 274	51. 492	1. 00 48. 44
15	ATOM 418	NH2	ARG 63	35. 295	17. 089	51. 268	1. 00 49. 50
		C .	ARG 63	39. 952	15. 006	57. 728	1. 00 50. 30
			ARG 63	39. 998	15. 478	58. 860	1. 00 49. 69
			SER 64	40. 987	14. 431	57. 128	1. 00 54. 64
			SER 64				1. 00 60. 87
20	ATOM 423						1. 00 60. 13
			SER 64				1. 00 62. 83
					15. 583	58. 398	1. 00 65. 69
•	ATOM 426		SER 64	42. 952	16. 584	57. 703	1. 00 65. 99
	ATOM 427		THR 65	42. 961	15. 530	59. 714	1. 00 71. 92
25	ATOM 428		CHR 65	43. 402	16. 649	60. 545	1. 00 77. 78
	ATOM 429		THR 65	44. 529	16. 194	61. 524	1. 00 78. 35
	ATOM 430		HR 65	44. 959	17. 309	62. 317	1. 00 79. 07
		CG2 T		45. 714	15. 611	60. 757	1. 00 79. 19
	ATOM 432	C T	HR 65	43. 839	17. 925	59. 817	1. 00 80. 90

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	ATOM 433	0	THR 65	45. 033	18. 188	59. 654	1. 00 80. 93
							1. 00 83. 72
	ATOM 435						1. 00 84. 56
	ATOM 436	CA	PRO 66	43. 162	19. 983	58. 661	1. 00 85. 58
5	ATOM 437	CB	PRO 66	41. 871	20. 254	57. 897	1. 00 85. 53
	ATOM 438	CG	PRO 66	40. 827	19. 776	58. 864	1. 00 85. 36
	ATOM 439	C	PRO 66	43. 468	21. 057	59. 710	1. 00 87. 07
	ATOM 440	0	PRO 66	42. 581	21. 812	60. 119	1. 00 87. 87
	ATOM 441	N	GLU 67	44. 726	21. 109	60. 144	1. 00 87. 71
10	ATOM 442	CA	GLU 67	45. 162	22. 055	61. 169	1. 00 87. 66
	ATOM 443	CB	GLU 67	46. 683	22. 238	61. 110	1. 00 88. 42
	ATOM 444	CG	GLU 67	47. 283	22. 824	62. 384	1. 00 89. 15
	ATOM 445	CD	GLU 67	46. 871	22. 058	63. 636	1. 00 89. 71
							1. 00 89. 95
15	ATOM 447	0E2	GLU 67	47. 728	21. 359	64. 217	1. 00 89. 51
		C	GLU 67				1. 00 86. 97
	ATOM 449						1. 00 86. 95
	ATOM 450		GLY 68				1. 00 85. 72
	ATOM 451	CA					1. 00 83. 56
20	ATOM 452						1. 00 82. 01
							1. 00 82. 39
							1. 00 79. 39
	ATOM 455	CA	SER 69	41. 469	24. 869	65. 537	1. 00 77. 31
0.5	ATOM 456	CB	SER 69	41. 855	23. 784	66. 542	1. 00 77. 69
25	ATOM 457	OG	SER 69	40. 877	23. 677	67. 561	1. 00 78. 20
	ATOM 458	C	SER 69	41. 118	26. 143	66. 294	1. 00 75. 21
	ATOM 459	0	SER 69	41. 993	26. 857	66. 784	1. 00 74. 23
	ATOM 460	N	GLU 70	39. 822	26. 413	66. 386	1. 00 73. 26
	ATOM 461	CA	GLU 70	39. 328	27. 581	67. 096	1. 00 71. 89

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	ATOM	462 · C	B GLU	70	38. 004	28. 042	66. 482	1. 00 73. 40
	ATOM	463 C	G GLU	70	37. 897	29. 544	66. 297	1. 00 77. 84
	ATOM	464 C	D GLU	70	38. 900	30. 073	65. 285	1. 00 80. 27
	ATOM	465 0]	E1 GLU	70	38. 763	29. 757	64. 082	1. 00 81. 41
5	ATOM	466 01	E2 GLU	70	39. 830	30. 801	65. 692	1. 00 81. 33
	ATOM	467 C	GLU	70	39. 107	27. 144	68. 543	1. 00 69. 48
	ATOM	468 0	GLU	70	38. 409	26. 163	68. 789	1. 00 69. 73
	ATOM	469 N	VAL	71	39. 701	27. 853	69. 499	1. 00 65. 92
	ATOM	470 CA	VAL	71	39. 536	27. 490	70. 904	1. 00 62. 64
10	ATOM 4	471 CF	8 VAL	71	40. 760	27. 909	71. 746	1. 00 61. 59
	ATOM 4	472 CC	1 VAL	71	41. 993	27. 156	71. 275	. 1. 00 61. 91
	ATOM 4	473 CC	2 VAL	71	40. 979	29. 406	71. 642	1. 00 61. 78
	ATOM 4	474 C	VAL	71	38. 278	28. 105	71. 510	1. 00 61. 05
	ATOM 4	475 0	VAL	71	37. 608	28. 919	70. 877	1. 00 61. 02
15	ATOM 4	476 N	GLY	72	37. 952	27. 700	72. 734	1. 00 59. 60
	ATOM 4		GLY	72	36. 769	28. 225	73. 390	1. 00 58. 10
	ATOM 4		GLY					1. 00 57. 74
	ATOM 4					25. 982	74. 006	1. 00 58. 27
	ATOM 4			73				1. 00 55. 55
20	ATOM 4							1. 00 54. 21
	ATOM 4							1. 00 57. 20
						27. 496	77. 424	1. 00 59. 78
	ATOM 4		1 ASP		35. 046	27. 830	77. 299	1. 00 61. 37
	ATOM 4		2 ASP		33. 324	27. 225	78. 529	1. 00 60. 87
25	ATOM 4	-	ASP		32. 599	26. 310	73. 994	1. 00 52. 36
	ATOM 4		ASP			27. 161	73. 406	1. 00 52. 44
	ATOM 4		PHE				73. 800	1. 00 49. 73
	ATOM 4		PHE					1. 00 46. 98
	ATOM 4	90 CB	PHE	74	32. 019	23. 571	71. 837	1. 00 46. 41

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	ATOM 491	CG PHE 74	33. 117	24. 179	71. 030	1. 00 47. 09
	ATOM 492	CD1 PHE 74	34. 335	24. 492	71. 618	1. 00 47. 62
	ATOM 493	CD2 PHE 74	32. 930	24. 452	69. 681	1. 00 47. 01
	ATOM 494	CE1 PHE 74	35. 359	25. 071	70. 874	1. 00 49. 47
5	ATOM 495	CE2 PHE 74	33. 943	25. 031	68. 924	1. 00 48. 12
	ATOM 496	CZ PHE 74	35. 161	25. 342	69. 520	1. 00 48. 82
	ATOM 497	C PHE 74	30. 316	23. 783	73. 601	1. 00 45. 68
	ATOM 498	0 PHE 74	30. 485	23. 382	74. 745	1. 00 46. 35
	ATOM 499	N LEU 75	29. 185	23. 615	72. 932	1. 00 45. 12
10	ATOM 500	CA LEU 75	28.064	22. 895	73. 501	1. 00 44. 80
	ATOM 501	CB LEU 75	26. 769	23. 686	73. 333	1. 00 43. 29
	ATOM 502	CG LEU 75	25. 535	23. 023	73. 959	1. 00 45. 05
	ATOM 503	CD1 LEU 75	25. 529	23. 278	75. 466	1. 00 41. 53
	ATOM 504	CD2 LEU 75	24. 259	23. 571	73. 326	1. 00 43. 45
15	ATOM 505	C LEU 75	27. 971	21. 598	72. 708	1. 00 46. 04
	ATOM 506	0 LEU 75	28. 087	21. 611	71. 479	1. 00 46. 97
	ATOM 507	N SER 76	27. 770	20. 484	73. 405	1. 00 45. 48
	ATOM 508	CA SER 76	27. 664	19. 189	72. 744	1. 00 43. 73
	ATOM 509	CB SER 76	28. 837	18. 295	73. 143	1. 00 43. 52
20	ATOM 510	OG SER 76	30. 040	18. 741	72. 551	1. 00 44. 64
	ATOM 511	C SER 76	26. 361	18. 469	73. 051	1. 00 41. 60
	ATOM 512	0 SER 76	26. 026	18. 242	74. 209	1. 00 40. 88
	ATOM 513	N LEU 77	25. 617	18. 130	72. 007	1. 00 41. 06
	ATOM 514	CA LEU 77	24. 369	17. 397	72. 175	1. 00 43. 50
25	ATOM 515	CB LEU 77	23. 281	17. 918	71. 225	1. 00 43. 84
	ATOM 516	CG LEU 77	22. 750	19. 346	71. 401	1. 00 45. 70
	ATOM 517	CD1 LEU 77	21. 587	19. 577	70. 442	1. 00 45. 96
	ATOM 518	CD2 LEU 77	22. 284	19. 550	72. 835	1. 00 46. 75
	ATOM 519	C LEU 77	24. 662	15. 933	71. 851	1. 00 43. 78

- 34 -ATOM 520 0 LEU 77 25. 529 15. 635 71.026 1. 00 43. 07 ATOM 521 N ASP 78 23. 946 15. 021 72. 496 1. 00 44. 50 ATOM 522 $\mathsf{C}\mathsf{A}$ ASP 78 24. 151 13. 604 72. 244 1. 00 44. 82 ATOM 523 CBASP 78 25. 126 13. 026 73. 271 1.00 44.71 5 ATOM 524 CG ASP 78 25. 597 11.628 72. 905 1. 00 45. 55 ATOM 525 OD1 ASP 78 24. 738 10. 750 72. 672 1.00 41.76 ATOM 526 OD2 ASP 78 26.828 11. 410 72. 853 1. 00 45. 32 ATOM 527 C ASP 78 22. 838 12. 829 72. 276 1. 00 44. 74 ATOM 528 0 ASP 78 22. 245 12. 633 73. 333 1. 00 45. 25 10 ATOM 529 N LEU 79 22. 385 12. 398 71. 107 1. 00 45. 72 LEU 79 ATOM 530 CA 21. 154 11.630 70. 994 1. 00 47. 25 ATOM 531 CBLEU 79 20. 137 12. 351 70. 116 1. 00 45. 37 ATOM 532 CG LEU 79 18.865 11. 530 69. 915 1. 00 43. 65 ATOM 533 CD1 LEU 79 18.067 11. 553 71. 200 1. 00 46. 42 15 ATOM 534 CD2 LEU 79 18. 045 12. 086 68. 777 1. 00 43. 81 ATOM 535 C LEU 79 21.491 10. 295 70. 354 1. 00 49. 50 ATOM 536 0 LEU 79 22.073 10. 249 69. 274 1. 00 49. 35 ATOM 537 GLY 80 N 21. 123 9. 207 71.016 1. 00 52. 24 ATOM 538 CA **GLY 80** 21. 421 7. 902 70.466 1. 00 56. 31 20 ATOM 539 С GLY 80 20.965 6. 833 71. 420 1. 00 59. 13 ATOM 540 GLY 80 20. 278 5. 896 71. 027 1. 00 60. 86 ATOM 541 N GLY 81 21. 360 6.966 72. 679 1. 00 62. 30 ATOM 542 CA GLY 81 20.940 6. 002 73. 674 1. 00 65. 60 ATOM 543 C GLY 81 19.551 6. 395 74. 137 1. 00 67. 84 ATOM 544 25 0 GLY 81 18. 936 7. 301 73. 564 1. 00 69. 00 ATOM 545 N THR 82 19. 047 5. 722 75. 165 1. 00 69. 33 ATOM 546 THR 82 CA 17. 726 6. 037 75. 695 1. 00 70. 36 ATOM 547 CBTHR 82 17. 110 4. 824 76. 418 1. 00 71. 43 ATOM 548 OG1 THR 82 18. 032 4. 332 77. 398 1.00 71.60

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CG2 THR 82 ATOM 549 16. 784 75. 420 1. 00 71. 87 ATOM 550 C THR 82 17. 846 7. 196 76. 679 1. 00 70. 10 ATOM 551 0 THR 82 16. 933 7. 458 77. 464 1. 00 71. 18 ATOM 552 N ASN 83 18. 981 7.887 76.625 1. 00 69. 08 ATOM 553 5 CA ASN 83 19. 232 9. 017 77. 508 1. 00 68. 14 ATOM 554 CBASN 83 20. 161 8. 584 78. 646 1. 00 69. 98 ATOM 555 CG ASN 83 19.862 9. 300 79. 948 1. 00 70. 80 ATOM 556 OD1 ASN 83 20. 627 9. 213 80. 909 1. 00 71. 46 ATOM 557 ND2 ASN 83 18. 739 10.004 79. 990 1. 00 72. 56 10 ATOM 558 ASN 83 C 19.866 10. 177 76. 738 1. 00 66. 16 ATOM 559 ASN 83 21.0500 10. 136 76. 407 1. 00 66. 52 ATOM 560 N PHE 84 19.073 11. 203 76. 447 1. 00 63. 41 ATOM 561 CA PHE 84 19. 567 12. 375 75. 728 1.00 60.93 ATOM 562 CB PHE 84 18.398 13. 227 75. 241 1. 00 61. 87 15 ATOM 563 CG PHE 84 18.817 14. 477 74. 528 1. 00 63. 55 ATOM 564 CD1 PHE 84 18. 419 15.724 74. 993 1. 00 63. 38 ATOM 565 CD2 PHE 84 19. 599 14. 409 73. 381 1. 00 64. 28 ATOM 566 CE1 PHE 84 18. 793 16.888 74. 325 1. 00 64. 07 ATOM 567 CE2 PHE 84 19.979 15. 568 72. 705 1. 00 65. 31 ATOM 568 20 PHE 84 CZ 19. 574 16.810 73. 179 1.00 64.75 ATOM 569 PHE 84 С 20. 442 13. 206 76. 658 1. 00 59. 07 ATOM 570 0 PHE 84 20.011 13. 582 77. 744 1. 00 59. 19 ATOM 571 N ARG 85 21.665 13. 500 76. 232 1. 00 57. 25 ATOM 572 CA ARG 85 22. 583 14. 272 77.064 1. 00 56. 05 ATOM 573 25 CBARG 85 23. 857 13. 467 77. 344 1. 00 56. 68 ATOM 574 ARG 85 CG 23.605 12. 044 77. 828 1. 00 58. 78 ATOM 575 CDARG 85 24.896 11. 367 78. 267 1. 00 59. 39 ATOM 576 NE ARG 85 25. 908 11. 348 77. 213 1. 00 59. 87 ATOM 577 CZARG 85 27. 068 11. 994 77. 282 1.00 60.09

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	ATOM 578	NH1 ARG 85	27. 366	- 30 12. 713	- 78. 357	1. 00 59. 50
	ATOM 579		27. 931	11. 920	76. 277	
	ATOM 580		22. 966	15. 602	76. 433	1. 00 00. 92
	ATOM 581	0 ARG 85	23. 038	15. 725	75. 209	1. 00 54. 93
5	ATOM 582		23. 211	16. 593	77. 288	1. 00 54. 93
	ATOM 583	CA VAL 86	23. 598	17. 935	76. 861	1. 00 53. 13
	ATOM 584		22. 425	18. 939	77. 003	1. 00 51. 01
	ATOM 585	CG1 VAL 86	22. 851	20. 313	76. 509	1. 00 51. 19
	ATOM 586	CG2 VAL 86	21. 216	18. 446	76. 225	1. 00 51. 33
10	ATOM 587	C VAL 86	24. 734	18. 381	77. 767	1. 00 49. 34
	ATOM 588	0 VAL 86	24. 613	18. 316	78. 989	1. 00 48. 07
	ATOM 589	N MET 87	25. 834	18. 835	77. 178	1. 00 49. 52
	ATOM 590	CA MET 87	26. 970	19. 260	77. 981	1. 00 50. 78
	ATOM 591	CB MET 87	27. 864	18. 054	78. 284	1. 00 52. 70
15	ATOM 592	CG MET 87	28. 572	17. 461	77. 072	1. 00 54. 49
	ATOM 593	SD MET 87	29. 005	15. 694	77. 269	1. 00 53. 62
	ATOM 594	CE MET 87	27. 839	14. 951	76. 090	1. 00 51. 63
	ATOM 595	C MET 87	27. 800	20. 363	77. 348	1. 00 50. 56
	ATOM 596	0 MET 87	27. 715	20. 616	76. 149	1. 00 50. 18
20	ATOM 597	N LEU 88	28. 605	21. 015	78. 178	1. 00 50. 90
	ATOM 598	CA LEU 88	29. 477	22. 093	77. 739	1. 00 52. 10
	ATOM 599	CB LEU 88	29. 278	23. 325	78. 631	1. 00 53. 23
	ATOM 600	CG LEU 88	30. 087	24. 580	78. 288	1. 00 54. 71
	ATOM 601	CD1 LEU 88	29. 618	25. 140	76. 951	1. 00 54. 33
25	ATOM 602	CD2 LEU 88	29. 920	25. 623	79. 390	1. 00 54. 33
	ATOM 603	C LEU 88	30. 914	21. 600	77. 847	1. 00 52. 33
	ATOM 604	0 LEU 88	31. 311	21. 048	78. 877	1. 00 53. 12
	ATOM 605	N VAL 89	31. 693	21. 795	76. 789	1. 00 52. 10
	ATOM 606	CA VAL 89	33. 078	21. 342	76. 788	1. 00 52. 46

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ATOM. 607 CB VAL 89 33. 241 20. 072 75. 882 1. 00 50. 52 ATOM 608 CG1 VAL 89 32. 289 20. 147 74. 710 1. 00 52. 35 ATOM 609 CG2 VAL 89 34. 674 19. 939 75. 388 1.00 46.86 ATOM 610 C VAL 89 34. 049 22. 433 76. 357 1.00 53.35 5 ATOM 611 0 VAL 89 33. 858 23.081 75. 336 1.00 54.69 ATOM 612 LYS 90 N 22. 625 35. 096 77. 151 1. 00 55. 22 ATOM 613 CA LYS 90 36. 100 23.640 76.868 1.00 56.94 ATOM 614 CBLYS 90 36. 656 24. 205 78. 181 1.00 57.66 ATOM 615 CG LYS 90 37. 642 25. 360 78.005 1. 00 58. 70 10 ATOM 616 CDLYS 90 38. 140 25. 909 79. 345 1. 00 59. 35 ATOM 617 CE LYS 90 36. 995 26. 399 1.00 60.64 80. 226 ATOM 618 LYS 90 NZ 36. 185 27. 462 79. 568 1. 00 61. 04 ATOM 619 C LYS 90 37. 237 23.078 76.019 1. 00 57. 63 ATOM 620 LYS 90 0 37. 921 22. 136 76. 417 1. 00 57. 69 ATOM 621 15 N VAL 91 37. 428 23. 670 74. 846 1. 00 58. 29 ATOM 622 CA VAL 91 38. 473 23. 254 73. 919 1. 00 57. 11 ATOM 623 CB VAL 91 37. 920 23. 136 72.480 1. 00 56. 48 ATOM 624 CG1 VAL 91 39.010 22. 661 71. 533 1. 00 55. 29 ATOM 625 CG2 VAL 91 36.741 22. 183 72. 459 1. 00 55. 52 ATOM 626 20 C VAL 91 39. 598 24. 279 73. 926 1. 00 57. 81 ATOM 627 0 VAL 91 39. 365 25. 466 73. 710 1. 00 59. 53 ATOM 628 N GLY 92 40.817 23. 819 74. 172 1. 00 58. 12 ATOM 629 CA GLY 92 41.947 24. 723 74. 200 1. 00 59. 69 ATOM 630 C **GLY 92** 43.047 24. 245 73. 286 1. 00 61. 78 25 ATOM 631 0 GLY 92 42. 821 23. 381 72. 448 1.00 61.06 ATOM 632 N GLU 93 44. 240 24. 803 73. 449 1. 00 65. 18 ATOM 633 GLU 93 CA 45. 373 24. 426 72.619 1. 00 69. 00 ATOM 634 CBGLU 93 45. 897 25. 646 71.866 1. 00 71. 56 ATOM 635 CG GLU 93 47. 082 25. 344 70.965 1. 00 75. 20

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				00		
	ATOM 636	6 CD GLU 93	47. 659	26. 591	70. 325	1. 00 78. 28
	ATOM 637	7 OE1 GLU 93	46. 893	27. 326	69. 659	1. 00 80. 05
	ATOM 638	3 OE2 GLU 93	48. 877	26. 834	70. 485	1. 00 79. 21
	ATOM 639	C GLU 93	46. 505	23. 822	73. 437	1. 00 71. 00
5	ATOM 640	0 GLU 93	47. 118	24. 500	74. 263	1. 00 70. 74
	ATOM 641	N GLY 94	46. 784	22. 544	73. 195	1. 00 72. 97
	ATOM 642	CA GLY 94	47. 849	21. 869	73. 916	1. 00 74. 44
	ATOM 643	C GLY 94	49. 078	21. 673	73. 052	1. 00 75. 82
	ATOM 644	0 GLY 94	49. 485	22. 577	72. 315	1. 00 76. 47
10	ATOM 645	N GLU 95	49. 682	20. 496	73. 145	1. 00 75. 73
	ATOM 646	CA GLU 95	50. 859	20. 195	72. 349	1. 00 76. 61
	ATOM 647	CB GLU 95	52. 023	19. 792	73. 249	1. 00 76. 93
	ATOM 648	CG GLU 95	52. 439	20. 891	74. 203	1. 00 78. 31
	ATOM 649	CD GLU 95	53. 614	20. 497	75. 065	1. 00 78. 40
15	ATOM 650	OE1 GLU 95	54. 715	20. 274	74. 514	1. 00 78. 51
	ATOM 651	OE2 GLU 95	53. 432	20. 408	76. 295	1. 00 78. 60
	ATOM 652	C GLU 95	50. 516	19. 071	71. 392	1. 00 76. 91
	ATOM 653	0 GLU 95	49. 833	18. 116	71. 764	1. 00 76. 81
	ATOM 654	N GLU 96	50. 987	19. 203	70. 155	1. 00 77. 78
20	ATOM 655	CA GLU 96	50. 733	18. 220	69. 105	1. 00 78. 07
	ATOM 656	CB GLU 96				1. 00 81. 32
	ATOM 657	CG GLU 96	52. 943	16. 930	69. 454	1. 00 85. 11
	ATOM 658	CD GLU 96	53. 541	17. 309	68. 101	1. 00 87. 05
	ATOM 659	OE1 GLU 96	53. 346	16. 551	67. 124	1. 00 88. 73
25	ATOM 660	OE2 GLU 96	54. 207	18. 365	68. 014	1. 00 87. 56
	ATOM 661	C GLU 96	49. 230	18. 025	68. 919	1. 00 75. 88
	ATOM 662	0 GLU 96	48. 784	17. 039	68. 327	1. 00 75. 92
	ATOM 663	N GLY 97	48. 456	18. 980	69. 427	1. 00 72. 88
	ATOM 664	CA GLY 97	47. 013	18. 910	69. 309	1. 00 69. 37

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	ATOM 665	C GLY	97 4	6. 296 1	9. 710 7	0. 380	1. 00 67. 02
	ATOM 666	0 GLY	97 4	6. 921 2	0. 230 7	1. 305	1. 00 67. 10
	ATOM 667	N GLN	98 4	4. 978 1	9. 811 7	0. 250	1. 00 64. 76
	ATOM 668	CA GLN	98 4	4. 166 2	0. 543 7	1. 211	1. 00 62. 45
5	ATOM 669	CB GLN	98 4	2. 872 2	1. 045 7	0. 562	1. 00 62. 69
	ATOM 670	CG GLN	98 4	3. 026 2	1. 908 6	9. 315	1. 00 64. 93
	ATOM 671	CD GLN	98 4	3. 191 2	1. 095 6	8. 046	1. 00 65. 89
	ATOM 672	OE1 GLN	98 4	4. 299 20	0. 684 6	7. 696	1. 00 65. 96
	ATOM 673	NE2 GLN	98 42	2. 079 20	0. 847 67	7. 353	1. 00 65. 22
10	ATOM 674	C GLN	98 43	3. 781 19	9. 630 72	2. 369	1. 00 61. 23
	ATOM 675	0 GLN	98 43	3. 880 18	3. 403 72	2. 269	1. 00 62. 18
	ATOM 676	N TRP	99 43	3. 356 20). 233 73	3. 473	1. 00 57. 45
	ATOM 677	CA TRP	99 42	2. 893 19). 459 74	l. 611	1. 00 54. 44
	ATOM 678	CB TRP	99 43	3. 639 19). 822 75	. 904	1. 00 55. 51
15	ATOM 679	CG TRP	99 43	. 770 21	. 291 76	. 211	1. 00 56. 94
	ATOM 680	CD2 TRP	99 42	. 763 22	. 151 76	. 756	1. 00 56. 03
	ATOM 681	CE2 TRP		. 345 23	. 426 76	. 922	. 00 57. 25
	ATOM 682	CE3 TRP		. 422 21	. 969 77	. 121	. 00 56. 67
	ATOM 683	CD1 TRP		. 892 22	. 062 76	. 068 1	. 00 56. 29
20	ATOM 684	NE1 TRP		. 647 23.	. 342 76	. 495 1	. 00 56. 55
	ATOM 685	CZ2 TRP		. 635 24.	. 516 77.	. 440 1	. 00 56. 53
	ATOM 686	CZ3 TRP S				_	. 00 56. 67
	ATOM 687	CH2 TRP 9					. 00 56. 70
	ATOM 688				756 74.		. 00 52. 04
25	ATOM 689						. 00 50. 70
	ATOM 690	N SER	100	40. 704	18. 981	75. 545	1. 00 49. 57
	ATOM 691	CA SER	100	39. 277		75. 715	
	ATOM 692	CB SER	100		18. 475		
	ATOM 693	OG SER	100	39. 055	17. 196	74. 315	1. 00 47. 27

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ATOM 722

CG LYS

104

28. 823

23. 450

83. 739

1. 00 59. 16

- 40 -ATOM 694 C SER 100 38. 860 18. 655 77.067 1.00 47.91 ATOM 695 0 SER 100 39. 569 17. 845 77.662 1.00 48.73 ATOM 696 N VAL 101 37. 718 19. 120 77. 558 1.00 47.53 ATOM 697 CA VAL 101 37. 225 18.684 78.852 1.00 47.86 ATOM 698 CBVAL 38. 102 101 19. 233 79. 995 1.00 47.92 ATOM 699 CG1 VAL 101 38. 160 20. 747 79. 923 1.00 49.02 CG2 VAL ATOM 700 101 37. 545 18. 783 81. 342 1.00 47.98 ATOM 701 C VAL 101 35. 784 19. 102 79. 101 1.00 48.77 ATOM 702 0 VAL 101 35. 391 20. 228 78. 798 1.00 49.05 ATOM 703 N LYS 102 18. 176 35. 004 79. 649 1.00 49.04 ATOM 704 CA LYS 102 33.607 18. 422 79. 969 1. 00 50. 31 ATOM 705 CBLYS 102 32. 875 17. 101 80. 220 1. 00 51. 15 ATOM 706 CG LYS 102 31. 385 17. 263 80. 452 1.00 52.57 ATOM 707 CDLYS 102 30.835 16. 229 81. 425 1. 00 56. 56 ATOM 708 CE LYS 102 30. 955 14.804 80. 908 1.00 57.06 ATOM 709 NZ LYS 102 30. 275 13.804 81. 787 1.00 58.08 ATOM 710 C LYS 102 33. 587 19. 254 81. 243 1. 00 51. 12 ATOM 711 0 LYS 102 34. 220 18.888 82. 234 1. 00 52. 47 ATOM 712 N THR 103 32. 859 20.366 81. 217 1.00 51.40 ATOM 713 CA THR 103 32. 774 21. 252 82. 373 1. 00 50. 47 ATOM 714 CB THR 103 33.004 22. 715 81. 965 1. 00 50. 28 ATOM 715 OG1 THR 103 31.992 23. 113 81.032 1. 00 51. 29 ATOM 716 CG2 THR 103 34. 368 22. 879 81. 324 1. 00 47. 52 ATOM 717 C THR 103 31. 416 21. 148 83. 048 1. 00 50. 90 ATOM 718 0 THR 103 31. 329 21.056 84. 268 1. 00 50. 91 ATOM 719 N LYS 104 30. 358 21. 162 82. 247 1. 00 52. 41 ATOM 720 CA LYS 104 29. 000 21.063 82. 770 1.00 54.04 ATOM 721 CB LYS 104 22. 436 28. 310 82. 714 1. 00. 57. 21

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	ATOM 723	CD	LYS	104	28. 138	24. 809	83. 576	1. 00 62. 54
	ATOM 724	CE	LYS	104	28. 398	25. 734	84. 766	1. 00 62. 99
	ATOM 725	NZ	LYS	104	27. 798	25. 217	86. 037	1. 00 64. 17
	ATOM 726	C	LYS	104	28. 215	20. 047	81. 948	1. 00 53. 79
5	ATOM 727	0	LYS	104	28. 411	19. 941	80. 740	1. 00 53. 53
	ATOM 728	N	HIS	105	27. 330	19. 299	82. 600	1. 00 53. 65
	ATOM 729	CA	HIS	105	26. 539	18. 295	81. 903	1. 00 55. 05
	ATOM 730	CB	HIS	105	27. 316	16. 972	81. 837	1. 00 55. 94
	ATOM 731	CG	HIS	105	27. 668	16. 397	83. 176	1. 00 55. 84
10	ATOM 732	CD2	HIS	105	28. 793	16. 501	83. 924	1. 00 55. 19
	ATOM 733	ND1	HIS	105	26. 803	15. 602	83. 897	1. 00 55. 83
	ATOM 734	CE1	HIS	105	27. 380	15. 241	85. 030	1. 00 56. 35
	ATOM 735	NE2	HIS	105	28. 589	15. 773	85. 071	1. 00 55. 64
	ATOM 736	C	HIS	105	25. 169	18. 074	82. 534	1. 00 56. 32
15	ATOM 737	0	HIS	105	24. 903	18. 535	83. 640	1. 00 56. 55
	ATOM 738	N	GLN	106	24. 302	17. 365	81. 817	1. 00 58. 21
	ATOM 739	CA.	GLN	106	22. 950	17. 090	82. 289	1. 00 60. 74
	ATOM 740	CB	GLN	106	22. 108	18. 367	82. 224	1. 00 61. 97
	ATOM 741	CG	GLN	106	20. 775	18. 285	82. 945	1. 00 64. 86
20	ATOM 742		GLN	106	20. 928	18. 379	84. 447	1. 00 67. 03
	ATOM 743	0E1		106	21. 447	19. 370	84. 969	1. 00 68. 82
	ATOM 744	NE2		106	20. 479	17. 348	85. 155	1. 00 67. 41
	ATOM 745		GLN	106	22. 322	16. 025	81. 396	1. 00 61. 62
	ATOM 746		GLN	106	22. 532	16. 027	80. 186	1. 00 62. 03
25	ATOM 747		MET	107	21. 550	15. 121	81. 990	1. 00 63. 03
	ATOM 748		MET	107	20. 900	14. 058	81. 232	1. 00 64. 74
	ATOM 749		MET	107	21. 322	12. 688	81. 769	1. 00 66. 23
	ATOM 750		MET	107	22. 821	12. 456	81. 786	1. 00 68. 74
	ATOM 751	SD N	MET	107	23. 248	10. 812	82. 388	1. 00 70. 84

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	ATOM 752	CE	MET	107	23. 427	9. 926	80. 853	1. 00 71. 13
	ATOM 753	C	MET	107	19. 385	14. 175	81. 313	1. 00 65. 81
	ATOM 754	0	MET	107	18. 837	14. 489	82. 369	1. 00 65. 52
	ATOM 755	N	TYR	108	18. 712	13. 915	80. 196	1. 00 66. 87
5	ATOM 756	CA	TYR	108	17. 258	13. 984	80. 143	1. 00 68. 20
	ATOM 757	CB	TYR	108	16. 800	15. 167	79. 286	1. 00 67. 20
	ATOM 758	CG	TYR	108	17. 436	16. 484	79. 660	1. 00 66. 35
	ATOM 759	CD1	TYR	108	18. 781	16. 731	79. 386	1. 00 65. 95
	ATOM 760	CE1	TYR	108	19. 380	17. 929	79. 746	1. 00 65. 76
10	ATOM 761	CD2	TYR	108	16. 702	17. 477	80. 307	1. 00 66. 24
	ATOM 762	CE2	TYR	108	17. 292	18. 683	80. 674	1. 00 65. 93
	ATOM 763	CZ	TYR	108	18. 633	18. 902	80. 391	1. 00 66. 14
	ATOM 764	ОН	TYR	108	19. 235	20. 083	80. 763	1. 00 64. 27
	ATOM 765	C	TYR	108	16. 706	12. 700	79. 549	1. 00 70. 20
15	ATOM 766	0	TYR	108	16. 995	12. 363	78. 404	1. 00 70. 55
	ATOM 767	N	SER	109	15. 912	11. 982	80. 331	1. 00 73. 54
	ATOM 768	CA	SER	109	15. 322	10. 739	79. 863	1. 00 76. 84
	ATOM 769	CB	SER	109	14. 524	10. 082	80. 992	1. 00 77. 63
	ATOM 770	0G	SER	109	15. 353	9. 837	82. 120	1. 00 78. 13
20	ATOM 771	C	SER	109	14. 419	11. 020	78. 664	1. 00 78. 98
	ATOM 772	0	SER	109	13. 936	12. 138	78. 486	1. 00 78. 51
	ATOM 773	N	ILE	110	14. 198	10. 002	77. 841	1. 00 82. 34
	ATOM 774		ILE					1. 00 86. 07
	ATOM 775		ILE		13. 892		75. 511	
25	ATOM 776		ILE		13. 092			1. 00 86. 56
	ATOM 777	CG1		110	15. 379		75. 275	1. 00 86. 19
	ATOM 778		ILE		16. 025	8. 612	74. 258	1. 00 86. 76
	ATOM 779		ILE		11. 916			1. 00 88. 58
	ATOM 780	0	ILE	110	11. 596	8. 606	77. 152	1. 00 88. 69

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	ATOM 78	1 N	PRO	111	11, 016	10 767	76 910	1. 00 91. 13
	ATOM 782		PRO					1. 00 91. 83
	ATOM 783							1. 00 93. 32
	ATOM 784		PRO					1. 00 93. 16
5	ATOM 785		PRO			12. 819		
	ATOM 786		PRO			9. 613		
	ATOM 787		PRO					1. 00 95. 40
	ATOM 788		GLU	112	7. 758			1. 00 93. 80
	ATOM 789		GLU	112		8. 185		
10	ATOM 790		GLU		5. 816	7. 611		
	ATOM 791		GLU			6. 971		
	ATOM 792		GLU	112	5. 316	5. 989		1. 00101. 10
	ATOM 793		GLU		5. 967	5. 012		
	ATOM 794				5. 113		73. 372	
15	ATOM 795		GLU		6. 508		74. 418	
	ATOM 796		GLU	112	6. 914	8. 545		1. 00100. 17
	ATOM 797	N	ASP			9. 859		1. 00101. 44
	ATOM 798	CA	ASP		5. 056		73. 499	1. 00102. 05
	ATOM 799	CB	ASP	113	4. 087		74. 038	
20	ATOM 800	CG	ASP	113	4. 682		75. 177	
	ATOM 801	OD1	ASP	113	4. 961	11. 913	76. 249	
	ATOM 802	0D2	ASP	113	4. 870	13. 716	74. 999	1. 00101. 99
	ATOM 803	C	ASP	113	6. 131	11. 282	72. 638	1. 00102. 09
	ATOM 804	0	ASP	113	5. 843	11. 789	71. 553	1. 00101. 96
25	ATOM 805	N	ALA	114	7. 368	11. 273	73. 126	1. 00102. 12
	ATOM 806	CA	ALA	114	8. 484	11. 869	72. 401	1. 00102. 09
	ATOM 807	CB	ALA	114	9. 590	12. 256	73. 377	1. 00101. 76
	ATOM 808	C	ALA	114	9. 022	10. 895	71. 358	1. 00102. 06
	ATOM 809	0	ALA	114	9. 763	11. 282	70. 455	1. 00101. 89

- 44 -ATOM 810 N MET 115 8.640 9.630 71. 491 1. 00102. 04 ATOM 811 CA MET 115 9. 081 8. 592 70. 569 1. 00102. 05 ATOM 812 CBMET 115 9. 466 7. 331 71. 346 1. 00102. 77 ATOM 813 CG MET 115 10.637 7. 509 72. 307 1. 00103. 47 ATOM 814 5 SD MET 115 12. 256 7. 549 71.502 1.00104.26 ATOM 815 CE MET 115 12. 740 5. 824 71. 638 1. 00103. 48 ATOM 816 C MET 115 8.004 8. 253 69. 538 1. 00101. 77 ATOM 817 0 MET 115 8. 268 8. 275 68. 337 1. 00102. 14 ATOM 818 N THR 116 6. 796 7.942 70.006 1. 00101. 14 10 ATOM 819 CA THR 116 5. 690 7. 590 69. 110 1.00100.36 ATOM 820 CB THR 116 4. 517 6. 927 69. 880 1. 00100. 42 ATOM 821 OG1 THR 116 5. 004 5. 805 70.625 1. 00100. 29 ATOM 822 CG2 THR 116 3. 441 6. 441 68. 911 1. 00100. 05 ATOM 823 C THR 116 5. 150 8.816 68. 379 1.00 99.62 ATOM 824 15 0 THR 116 4. 423 8. 694 67. 391 1. 00 99. 72 ATOM 825 N GLY 117 5. 510 9.996 68.870 1. 00 98. 62 ATOM 826 CA GLY 117 5. 048 11. 224 68. 252 1.00 97.42 ATOM 827 C GLY 117 5. 619 11. 447 66.866 1. 00 96. 48 ATOM 828 0 GLY 117 5. 746 10. 511 66.074 1. 00 96. 38 ATOM 829 20 N THR 118 5. 962 12.696 66. 570 1. 00 95. 25 ATOM 830 CA THR 118 6. 521 13.050 65. 273 1.00 93.78 ATOM 831 CB THR 118 5. 679 14. 133 64. 578 1. 00 93. 57 ATOM 832 OG1 THR 118 5. 735 15. 343 65. 342 1. 00 93. 50 ATOM 833 CG2 THR 118 4. 234 13.685 64. 457 1. 00 93. 65 ATOM 834 25 C THR 118 7. 936 13. 583 65. 440 1. 00 92. 67 ATOM 835 0 THR 118 8. 335 13. 976 66. 537 1. 00 92. 39 ATOM 836 N ALA 119 8.687 13. 593 64. 343 1. 00 91. 30 ATOM 837 CAALA 119 10.058 14.084 64. 356 1.00 90.00 ATOM 838 CB ALA 119 10. 643 14. 031 62. 956 1. 00 89. 81

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						10		
	ATOM 839) C	ALA	119	10. 066	15. 513	64. 867	1. 00 89. 21
	ATOM 840	0	ALA	119	11. 045	15. 972	65. 455	1. 00 88. 98
	ATOM 841	N	GLU	120	8. 959	16. 210	64. 636	1. 00 88. 61
	ATOM 842	CA	GLU	120	8. 819	17. 593	65. 063	1. 00 87. 61
5	ATOM 843	СВ	GLU	120	7. 505	18. 177	64. 536	1. 00 87. 74
	ATOM 844	CG	GLU	120	7. 138	17. 763	63. 112	1. 00 86. 31
	ATOM 845	CD	GLU	120	8. 269	17. 956	62. 120	1. 00 85. 84
	ATOM 846	0E1	GLU	120	8. 884	19. 042	62. 113	1. 00 84. 76
	ATOM 847	0E2	GLU	120	8. 535	17. 020	61. 336	1. 00 85. 71
10	ATOM 848	C	GLU	120	8. 837	17. 658	66. 588	1. 00 86. 71
	ATOM 849	0	GLU	120	9. 610	18. 412	67. 179	1. 00 86. 71
	ATOM 850	N	MET	121	7. 980	16. 859	67. 216	1. 00 85. 74
	ATOM 851	CA	MET	121	7. 895	16. 817	68. 671	1. 00 84. 85
	ATOM 852	CB	MET	121	6. 798	15. 842	69. 111	1. 00 84. 04
15	ATOM 853	CG	MET	121	5. 390	16. 273	68. 740	1. 00 81. 88
	ATOM 854	SD	MET	121	4. 152	15. 078	69. 268	1. 00 80. 83
	ATOM 855	CE	MET	121	3. 772	14. 283	67. 730	1. 00 78. 55
	ATOM 856	C	MET	121	9. 226	16. 397	69. 286	1. 00 84. 73
	ATOM 857		MET	121	9. 687	17. 003	70. 255	1. 00 84. 87
20	ATOM 858				9. 839	15. 360	68. 717	1. 00 84. 21
				122				1. 00 83. 20
				122	11. 711	13. 847	68. 221	1. 00 83. 29
	ATOM 861	CG	LEU	122	12. 966	13. 109	68. 697	1. 00 83. 07
	ATOM 862	CD1	LEU	122	12. 612	12. 232	69. 885	1. 00 82. 78
25	ATOM 863	CD2	LEU	122	13. 533	12. 261	67. 572	1. 00 82. 52
	ATOM 864	C	LEU	122	12. 110	15. 980	69. 448	1. 00 82. 61
	ATOM 865		LEU	122	12. 546	16. 204	70. 575	1. 00 82. 47
	ATOM 866		PHE	123	12. 467	16. 694	68. 385	1. 00 82. 28
	ATOM 867	CA]	PHE	123	13. 414	17. 794	68. 512	1. 00 82. 09

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	ATOM 868	CB PHE	123	13. 898	18. 251	67. 136	1. 00 82. 08
	ATOM 869	CG PHE	123	14. 948	17. 357	66. 547	1. 00 81. 61
	ATOM 870	CD1 PHE	123	14. 616	16. 098	66. 060	1. 00 81. 34
	ATOM 871	CD2 PHE	123	16. 281	17. 756	66. 523	1. 00 81. 33
5	ATOM 872	CE1 PHE	123	15. 594	15. 246	65. 559	1. 00 80. 67
	ATOM 873	CE2 PHE	123	17. 268	16. 912	66. 026	1. 00 81. 58
	ATOM 874	CZ PHE	123	16. 923	15. 653	65. 543	1. 00 81. 33
	ATOM 875	C PHE	123	12. 834	18. 964	69. 288	1. 00 81. 98
	ATOM 876	0 PHE	123	13. 570	19. 838	69. 747	1. 00 81. 74
10	ATOM 877	N ASP	124	11. 512	18. 980	69. 429	1. 00 82. 09
	ATOM 878	CA ASP	124	10. 852	20. 028	70. 195	1. 00 82. 29
	ATOM 879	CB ASP	124	9. 329	19. 909	70. 073	1. 00 81. 96
	ATOM 880	CG ASP	124	8. 731	20. 961	69. 157	1. 00 81. 56
	ATOM 881	OD1 ASP	124	7. 510	20. 897	68. 901	1. 00 81. 25
15	ATOM 882	OD2 ASP	124	9. 477	21. 855	68. 701	1. 00 80. 94
	ATOM 883		124	11. 279	19. 808	71. 641	1. 00 82. 22
	ATOM 884		124	11. 819	20. 707	72. 287	1. 00 81. 61
	ATOM 885		125	11. 047	18. 595	72. 133	1. 00 82. 59
	ATOM 886	CA TYR	125	11. 420	18. 233	73. 494	1. 00 83. 66
20	ATOM 887	CB TYR	125	11. 048	16. 771	73. 767	1. 00 85. 84
	ATOM 888	CG TYR	125	11. 533			1. 00 88. 74
	ATOM 889	CD1 TYR	125		15. 590	7 5. 209	1. 00 89. 83
	ATOM 890	CE1 TYR	125	13. 222	15. 110	76. 437	1. 00 91. 28
	ATOM 891	CD2 TYR		10. 770	16. 399	76. 257	1. 00 90. 41
25	ATOM 892	CE2 TYR	125	11. 221	15. 926	77. 493	1. 00 91. 86
	ATOM 893	CZ TYR	125	12. 448	15. 281	77. 574	1. 00 92. 09
	ATOM 894	OH TYR	125	12. 896	14. 807	78. 789	1. 00 93. 08
	ATOM 895	C TYR	125	12. 917	18. 451	73. 704	1. 00 82. 86
	ATOM 896	0 TYR	125	13. 352	18. 829	74. 792	1. 00 82. 74

- 47 -ATOM 897 N ILE 18. 215 126 13. 701 72. 655 1. 00 81. 74 ATOM 898 CA ILE 126 15. 146 18. 398 72. 727 1.00 80.58 ATOM 899 CB ILE 126 15. 824 18.005 71. 397 1.00 79.32 ATOM 900 CG2 ILE 126 17. 277 18. 443 71. 398 1. 00 78. 57 5 ATOM 901 CG1 ILE 126 15. 719 16. 494 71. 194 1. 00 78. 47 ATOM 902 CD1 ILE 126 16. 408 15. 993 69. 946 1. 00 78. 42 ATOM 903 C ILE 126 15. 479 19.852 73. 047 1. 00 80. 87 ATOM 904 0 ILE 126 16. 334 20. 133 73.887 1.00 79.71 ATOM 905 N SER 127 14. 799 20. 772 72. 370 1.00 81.80 10 ATOM 906 CA SER 127 15. 018 22. 196 72. 594 1.00 82.44 ATOM 907 CB SER 127 14. 160 23. 021 71. 636 1. 00 82. 62 ATOM 908 0G SER 127 14. 559 22.807 70. 294 1. 00 83. 20 ATOM 909 C SER 127 14. 668 22. 543 74. 034 1. 00 82. 44 ATOM 910 0 SER 127 15. 318 23. 382 74.660 1.00 81.86 ATOM 911 15 N GLU 128 13.636 21. 884 74. 553 1.00 83.04 ATOM 912 CA GLU 128 13. 202 22. 106 75. 927 1. 00 83. 79 ATOM 913 CB GLU 128 11. 944 21. 289 76. 232 1.00 84.79 ATOM 914 CG GLU 128 11. 408 21. 490 77. 645 1. 00 86. 70 ATOM 915 CD GLU 128 10. 425 20. 409 78. 061 1. 00 88. 14 ATOM 916 20 OE1 GLU 128 9.408 20. 222 77. 357 1.00 88.36 ATOM 917 OE2 GLU 128 10.672 19. 747 79. 094 1.00 88.06 ATOM 918 C GLU 128 14. 318 21.686 76. 877 1. 00 83. 42 ATOM 919 0 GLU 128 14. 483 22. 261 77. 952 1. 00 84. 16 ATOM 920 N CYS 129 15.081 20. 675 76. 475 1. 00 82. 77 ATOM 921 25 CA CYS 129 16. 177 20. 179 77. 295 1.00 81.21 ATOM 922 CBCYS 129 16. 554 18. 760 76. 873 1. 00 81. 07 ATOM 923 SG CYS 129 15. 206 17. 569 77. 006 1. 00 80. 63 ATOM 924 C CYS 129 17. 391 21.089 77. 178 1.00 80.64 ATOM 925 0 CYS 129 18. 092 21. 330 78. 160 1. 00 79. 84

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	ATOM 926	N ILE	130	17. 644	21. 591	75. 975	1. 00 80. 16
	ATOM 927	CA ILE	130	18. 782	22. 475	75. 775	1. 00 80. 33
	ATOM 928	CB ILE	130	18. 944	22. 860	74. 298	1. 00 79. 59
	ATOM 929	CG2 ILE	130	20. 253	23. 614	74. 102	1. 00 79. 29
5	ATOM 930	CG1 ILE	130	18. 933	21. 599	73. 436	1. 00 79. 00
	ATOM 931	CD1 ILE	130	19. 069	21. 860	71. 958	1. 00 79. 73
	ATOM 932	C ILE	130	18. 559	23. 735	76. 595	1. 00 80. 49
	ATOM 933	0 ILE	130	19. 475	24. 241	77. 239	1. 00 80. 22
	ATOM 934	N SER	131	17. 326	24. 229	76. 574	1. 00 81. 09
10	ATOM 935	CA SER	131	16. 970	25. 428	77. 320	1. 00 82. 28
	ATOM 936	CB SER	131	15. 525	25. 826	77. 006	1. 00 83. 15
	ATOM 937	OG SER	131	14. 641	24. 736	77. 195	1. 00 82. 88
	ATOM 938	C SER	131	17. 136	25. 195	78. 820	1. 00 82. 33
	ATOM 939	0 SER	131	17. 843	25. 940	79. 501	1. 00 82. 07
15	ATOM 940	N ASP	132	16. 478	24. 155	79. 322	1. 00 82. 42
	ATOM 941	CA ASP	132	16. 540	23. 792	80. 735	1. 00 82. 24
	ATOM 942	CB ASP	132	15. 893	22. 411	80. 934	1. 00 83. 24
	ATOM 943	CG ASP	132	15. 836	21. 981	82. 393	1. 00 83. 66
	ATOM 944	OD1 ASP	132	15. 165	20. 963	82. 678	1. 00 83. 28
20	ATOM 945	OD2 ASP		16. 458	22. 645	83. 250	1. 00 83. 85
	ATOM 946					81. 200	
	ATOM 947	0 ASP	132	18. 324	24. 293	82. 270	1. 00 82. 12
	ATOM 948	N PHE	133	18. 866	23. 193	80. 383	1. 00 80. 65
	ATOM 949	CA PHE	133	20. 286	23. 118	80. 698	1. 00 79. 47
25	ATOM 950	CB PHE	133	21. 033	22. 331	79. 616	1. 00 77. 80
	ATOM 951	CG PHE	133	22. 528	22. 391	79. 750	1. 00 75. 86
	ATOM 952	CD1 PHE	133	23. 178	21. 695	80. 761	1. 00 75. 50
	ATOM 953	CD2 PHE	133	23. 284	23. 179	78. 889	1. 00 75. 39
	ATOM 954	CE1 PHE	133	24. 562	21. 785	80. 914	1. 00 74. 78

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	ATOM 955	CE2	PHE	133	24. 667	23. 275	79. 035	1. 00 74. 59
	ATOM 956	CZ	PHE	133	25. 305	22. 578	80. 049	1. 00 74. 18
	ATOM 957	C	PHE	133	20. 876	24. 519	80. 786	1. 00 79. 33
	ATOM 958	0	PHE	133	21. 690	24. 810	81. 659	1. 00 79. 06
5	ATOM 959	N	LEU	134	20. 459	25. 382	79. 869	1. 00 79. 23
	ATOM 960	CA	LEU	134	20. 951	26. 748	79. 828	1. 00 79. 59
	ATOM 961	CB	LEU	134	20. 482	27. 412	78. 534	1. 00 79. 43
	ATOM 962	CG	LEU	134	21. 043	26. 703	77. 297	1. 00 78. 61
	ATOM 963	CD1	LEU	134	20. 401	27. 247	76. 032	1. 00 78. 47
10	ATOM 964	CD2	LEU	134	22. 554	26. 878	77. 264	1. 00 77. 75
	ATOM 965	C	LEU	134	20. 524	27. 565	81. 043	1. 00 79. 41
	ATOM 966	0	LEU	134	21. 324	28. 310	81. 609	1. 00 78. 74
	ATOM 967	N	ASP	135	19. 268	27. 423	81. 448	1. 00 80. 16
	ATOM 968	CA	ASP	135	18. 780	28. 152	82. 609	1. 00 80. 92
15	ATOM 969	CB	ASP	135	17. 271	27. 966	82. 777	1. 00 80. 81
	ATOM 970	CG	ASP	135	16. 474	28. 778	81. 783	1. 00 81. 08
	ATOM 971				16. 801	29. 970	81. 599	1. 00 82. 67
	ATOM 972	OD2	ASP	135	15. 517	28. 234	81. 195	1. 00 81. 12
	ATOM 973	C	ASP	135	19. 486	27. 686	83. 872	1. 00 81. 80
20	ATOM 974	0	ASP	135	20. 090	28. 490	84. 578	1. 00 82. 12
	ATOM 975							1. 00 82. 43
	ATOM 976	CA 1	LYS	136	20. 041	25. 811	85. 333	1. 00 83. 25
	ATOM 977	CB 1	LYS	136	19. 750	24. 307	85. 418	1. 00 82. 64
	ATOM 978	CG 1	LYS	136	18. 288	23. 970	85. 677	1. 00 82. 57
25	ATOM 979	CD 1	LYS	136	18. 095	22. 487	85. 952	1. 00 82. 49
	ATOM 980	CE I	LYS	136	16. 630	22. 154	86. 182	1. 00 82. 31
	ATOM 981	NZ I	LYS	136	16. 053	22. 914	87. 323	1. 00 82. 43
	ATOM 982	C I	LYS	136	21. 548	26. 044	85. 429	1. 00 84. 12
	ATOM 983	0 I	LYS	136	22. 185	25. 610	86. 390	1. 00 84. 51

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	ATOM	984 N	Н	IS	137	22	. 119	26	. 727	84	. 442	1. 00	85. 0	8
	ATOM	985 C	A H	IS	137	23	. 551	27	. 010	84	. 450	1. 00	86. 2	7
	ATOM	986 C	В Н	IS	137	24.	. 280	26	. 115	83	. 438	1. 00	86. 7	4
	ATOM	987 C	G H	IS	137	24.	. 169	24.	649	83.	730	1. 00	87. 0	4
5	ATOM	988 CI	D2 H	IS	137	25.	. 112	23.	. 729	84.	047	1. 00	86. 4	4
	ATOM	989 NI	01 H	IS	137	22.	968	23.	971	83.	708	1. 00	87. 5	1
	ATOM	990 CI	E1 H1	IS	137	23.	176	22.	699	83.	999	1. 00	86. 59	9
	ATOM	991 NF	E2 H	[S	137	24.	468	22.	526	84.	209	1. 00	86. 38	5
	ATOM	992 C	HI	S	137	23.	820	28.	476	84.	123	1. 00	87. 1	1
10	ATOM	993 0	HI	S	137	24.	943	28.	842	83.	776	1. 00	86. 73	3
	ATOM	994 N	GI	.N	138	22.	784	29.	307	84.	249	1. 00	88. 4	I
	ATOM	995 CA	GI.	N	138	22.	883	30.	736	83.	955	1. 00	89. 43	}
	ATOM	996 CB	GL	N :	138	23.	469	31.	512	85.	140	1. 00	90. 47	7
	ATOM	997 CG	GL	N :	138	22.	654	31.	451	86.	419	1. 00	92. 10)
15	ATOM	998 CD	GL	N I	138	22.	738	30.	099	87.	095	1. 00	93. 09	•
	ATOM	999 OE	1 GL	N]	138	23.	829	29.	598	87.	372	1. 00	93. 35	i
•	ATOM	1000	· NE2	GLN	138		21. 58	4	29. 50	01	87. 37	1 1.	00 93	. 71
	ATOM	1001	С	GLN	138		23. 77	9	30. 93	31	82. 74	7 1.	00 89	. 90
	ATOM	1002	0	GLN	138		24. 92	2	31. 37	76	82. 87	5 1.	00 89	. 53
20	ATOM	1003	N	MET	139		23. 26	2	30. 59	91	81. 57	3 1.	00 89	. 97
	ATOM	1004	CA	MET	139		24. 04		30. 72	25	80. 359	9 1.	00 90	. 27
	ATOM	1005		MET	139		24. 99	5	29. 52	29	80. 23	5 1. (00 90	. 82
	ATOM	1006	CG	MET	139		26. 31	4	29. 83	8	79. 542	2 1. (00 91	. 26
	ATOM	1007	SD	MET	139		27. 52	6	28. 50	8	79. 736	3 1. (00 90.	. 73
25	ATOM	1008	CE	MET	139		28. 30	3	28. 97	4	81. 303	3 1. 0	00 91.	. 08
	ATOM	1009	С	MET	139		23. 13'	7	30. 82	0	79. 140	1. (00 90.	17
	ATOM	1010	0	MET	139		23. 610) ;	30. 89	4	78. 006	1. (00 90.	11
	ATOM	1011	N	LYS	140		21. 829) ;	30. 82	9 ′	79. 380	1. (0 89.	92
	ATOM	1012	CA	LYS	140		20. 85	l :	30. 92	1 7	78. 300	1. 0	0 89.	78

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	ATOM	1013	CB	LYS	140	19. 434	30. 922	78. 874	1. 00 89. 37
	ATOM	1014	CG	LYS	140	18. 357	31. 239	77. 852	1. 00 89. 17
	ATOM	1015	CD	LYS	140	16. 972	31. 055	78. 438	1. 00 89. 06
	ATOM	1016	CE	LYS	140	16. 688	29. 588	78. 675	1. 00 88. 66
5	ATOM	1017	NZ	LYS	140	16. 797	28. 822	77. 406	1. 00 88. 73
	ATOM	1018	C	LYS	140	21.067			
	ATOM	1019	0	LYS	140	20. 593	32. 278	76. 334	1. 00 89. 28
	ATOM	1020	N	HIS	141	21. 794	33. 133	78. 037	1. 00 90. 38
	ATOM	1021	CA	HIS	141	22. 082	34. 401	77. 376	1. 00 90. 81
10	ATOM	1022	CB	HIS	141	22. 222	35. 506	78. 427	1. 00 90. 98
	ATOM	1023	CG	HIS	141	23. 294	35. 243	79. 443	1. 00 91. 18
	ATOM	1024	CD2	2 HIS	141	24. 520	35. 794	79. 610	1. 00 91. 04
	ATOM	1025	ND 1	HIS	141	23. 163	34. 294	80. 434	1. 00 91. 11
	ATOM	1026	CEI	HIS	141	24. 262	34. 273	81. 168	1. 00 91. 45
15	ATOM	1027	NE2	HIS	141	25. 102	35. 174	80. 688	1. 00 90. 96
	ATOM	1028	C	HIS	141	23. 349	34. 367	76. 516	1. 00 90. 72
	ATOM	1029	0	HIS	141	24. 048	35. 374	76. 399	1. 00 91. 00
	ATOM	1030	N	LYS	142	23. 648	33. 220	75. 912	1. 00 90. 17
	ATOM	1031	CA	LYS	142	24. 845	33. 109	75. 082	1. 00 89. 12
20	ATOM	1032	CB	LYS	142	26. 000	32. 529	75. 908	1. 00 89. 54
	ATOM	1033		LYS	142	26. 424	33. 406	77. 079	1. 00 90. 51
	ATOM	1034	CD	LYS	142	27. 490	32. 730	77. 926	1. 00 91. 91
	ATOM	1035	CE	LYS	142	27. 867	33. 579	79. 131	1. 00 92. 42
	ATOM	1036	NZ	LYS	142	28. 820	32. 863	80. 026	1. 00 92. 34
25	ATOM	1037	С	LYS	142	24. 643	32. 276	73. 815	1. 00 87. 58
	ATOM	1038	0	LYS	142	23. 763	31. 418	73. 749	1. 00 87. 74
	ATOM	1039	N	LYS	143	25. 465	32. 554	72. 808	1. 00 85. 65
	ATOM	1040	CA	LYS	143	25. 414	31. 849	71. 532	1. 00 83. 45
	ATOM	1041	CB	LYS	143	25. 052	32. 819	70. 402	1. 00 83. 10

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	ATOM	1042	CG	LYS	143	25. 199	32. 262	68. 988	1. 00 82. 55
	ATOM	1043	CD	LYS	143	24. 890	33. 339	67. 951	1. 00 82. 36
	ATOM	1044	CE	LYS	143	25. 289	32. 922	66. 540	1. 00 82. 46
	ATOM	1045	NZ	LYS	143	24. 519	31. 749	66. 045	1. 00 82. 29
5	ATOM	1046	С	LYS	143	26. 790	31. 252	71. 283	1. 00 82. 32
	ATOM	1047	0	LYS	143	27. 751	31. 974	71. 002	1. 00 82. 33
	ATOM	1048	N	LEU	144	26. 884	29. 932	71. 409	1. 00 79. 90
	ATOM	1049	CA	LEU	144	28. 146	29. 233	71. 198	1. 00 77. 12
	ATOM	1050	CB	LEU	144	28. 653	28. 634	72. 517	1. 00 78. 89
10	ATOM	1051	CG	LEU	144	29. 417	29. 543	73. 491	1. 00 80. 11
	ATOM	1052	CD	1 LEU	144	28. 560	30. 727	73. 924	1. 00 81. 77
	ATOM	1053	CD	2 LEU	144	29. 836	28. 721	74. 698	1. 00 80. 96
	ATOM	1054	С	LEU	144	27. 993	28. 132	70. 156	1. 00 73. 23
	ATOM	1055	0	LEU	144	26. 876	27. 742	69. 810	1. 00 72. 89
15	ATOM	1056	N	PRO	145	29. 119	27. 628	69. 628	1. 00 70. 01
	ATOM	1057	CD	PRO	145	30. 498	28. 104	69. 833	1. 00 68. 83
	ATOM	1058	CA	PRO	145	29. 081	26. 565	68. 621	1. 00 67. 77
	ATOM	1059	CB	PRO	145	30. 555	26. 356	68. 285	1. 00 68. 79
	ATOM	1060	CG	PRO	145	31. 159	27. 706	68. 542	1. 00 69. 21
20	ATOM	1061	C	PR0	145	28. 434	25. 299	69. 181	1. 00 65. 49
	ATOM	1062	0	PRO	145	28. 615	24. 963	70. 351	1. 00 64. 23
	ATOM	1063	N	LEU	146	27. 677	24. 603	68. 340	1. 00 63. 31
	ATOM	1064	CA	LEU	146	27. 007	23. 383	68. 757	1. 00 61. 72
	ATOM	1065	CB	LEU	146	25. 492	23. 532	68. 602	1. 00 62. 15
25	ATOM	1066	CG	LEU	146	24. 678	22. 285	68. 945	1. 00 62. 90
	ATOM	1067	CD1	LEU	146	25. 011	21. 842	70. 353	1. 00 64. 57
	ATOM	1068	CD2	LEU	146	23. 194	22. 577	68. 817	1. 00 65. 06
	ATOM	1069	C	LEU	146	27. 473	22. 152	67. 985	1. 00 59. 94
	ATOM	1070	0	LEU	146	27. 342	22. 086	66. 763	1. 00 59. 04

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	ATOM	1071	N	GLY	147	28. 028	21. 189	68. 721	1. 00 58. 65
	ATOM	1072	CA	GLY	147	28. 492	19. 939	68. 136	1. 00 54. 15
	ATOM	1073	С	GLY	147	27. 444	18. 891	68. 465	1. 00 49. 71
	ATOM	1074	0	GLY	147	27. 175	18. 628	69. 635	1. 00 50. 70
5	MOTA	1075	N	PHE	148	26. 854	18. 287	67. 440	1. 00 46. 12
	ATOM	1076	CA	PHE	148	25. 795	17. 297	67. 635	1. 00 42. 39
	ATOM	1077	CB	PHE	148	24. 610	17. 675	66. 740	1. 00 39. 68
	ATOM	1078	CG	PHE	148	23. 366	16. 864	66. 977	1. 00 38. 24
	ATOM	1079	CD1	PHE	148	22. 326	16. 901	66. 056	1. 00 36. 04
10	ATOM	1080	CD2	PHE	148	23. 212	16. 102	68. 132	1. 00 36. 13
	ATOM	1081	CE1	PHE	148	21. 148	16. 194	66. 279	1. 00 38. 53
	ATOM	1082	CE2	PHE	148	22. 042	15. 395	68. 365	1. 00 35. 28
	ATOM	1083	CZ	PHE	148	21. 005	15. 440	67. 437	1. 00 37. 48
	ATOM	1084	С	PHE	148	26. 197	15. 840	67. 354	1. 00 41. 67
15	ATOM	1085	0	PHE	148	26. 463	15. 475	66. 205	1. 00 42. 24
	ATOM	1086	N	THR	149	26. 247	15. 013	68. 398	1. 00 40. 23
	ATOM	1087	CA	THR	149	26. 562	13. 593	68. 222	1. 00 36. 30
	ATOM	1088	CB	THR	149	27. 281	13. 001	69. 442	1. 00 36. 36
	ATOM	1089	0G1	THR	149	28. 580	13. 597	69. 560	1. 00 37. 54
20	ATOM	1090	CG2	THR	149	27. 444	11. 492	69. 286	1. 00 37. 01
	ATOM	1091	С	THR	149	25. 212	12. 909	68. 039	1. 00 34. 65
	ATOM	1092	0	THR	149	24. 412	12. 836	68. 967	1. 00 31. 13
	ATOM	1093	N	PHE	150	24. 972	12. 422	66. 825	1. 00 33. 67
	ATOM	1094	CA	PHE	150	23. 714	11. 782	66. 456	1. 00 34. 60
25	ATOM	1095	CB	PHE	150	23. 061	12. 614	65. 336	1. 00 32. 78
	ATOM	1096	CG	PHE	150	21. 739	12. 086	64. 854	1. 00 30. 57
	ATOM	1097	CD1	PHE	150	21. 625	11. 513	63. 595	1. 00 30. 43
	ATOM	1098	CD2	PHE	150	20. 598	12. 213	65. 637	1. 00 31. 90
	ATOM	1099	CE1	PHE	150	20. 382	11. 076	63. 115	1. 00 34. 54

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	ATOM	1100	CE	2 PHE	150	19. 356	11. 783	65. 176	1. 00 30. 63
	ATOM	1101	CZ	PHE	150	19. 241	11. 213	63. 913	1. 00 32. 01
	ATOM	1102	C	PHE	150	24. 011	10. 358	65. 991	1. 00 35. 95
	ATOM	1103	0	PHE	150	24. 369	10. 128	64. 836	1. 00 38. 42
5	ATOM	1104	N	SER	151	23. 843	9. 412	66. 908	1. 00 36. 96
	MOTA	1105	CA	SER	151	24. 129	7. 995	66. 680	1. 00 34. 37
	MOTA	1106	CB	SER	151	24. 186	7. 271	68. 025	1. 00 35. 80
	MOTA	1107	0G	SER	151	25. 111	7. 897	68. 892	1. 00 39. 97
	ATOM	1108	С	SER	151	23. 189	7. 228	65. 770	1. 00 32. 05
10	ATOM	1109	0	SER	151	22. 537	6. 292	66. 215	1. 00 32. 11
	ATOM	1110	N	PHE	152	23. 110	7. 611	64. 505	1. 00 31. 41
	ATOM	1111	CA	PHE	152	22. 253	6. 902	63. 563	1. 00 31. 81
	ATOM	1112	CB	PHE	152	20. 824	7. 464	63. 570	1. 00 34. 43
	ATOM	1113	CG	PHE	152	20. 149	7. 372	64. 904	1. 00 34. 95
15	ATOM	1114	CD1	PHE	152	20. 278	8. 401	65. 838	1. 00 32. 95
	ATOM	1115	CD2	PHE	152	19. 439	6. 228	65. 256	1. 00 35. 34
	ATOM	1116	CE 1	PHE	152	19. 713	8. 291	67. 108	1. 00 35. 00
	ATOM	1117	CE2	PHE	152	18. 868	6. 102	66. 526	1. 00 35. 79
	ATOM	1118	CZ	PHE	152	19. 005	7. 135	67. 454	1. 00 38. 15
20	ATOM	1119		PHE	152	22. 845		62. 171	1. 00 31. 95
	ATOM	1120	0	PHE	152	23. 727	7. 831	61. 921	1. 00 31. 72
	ATOM	1121	N	PRO	153	22. 386	6. 164	61. 247	1. 00 32. 44
	ATOM	1122	CD	PRO	153	21. 374	5. 098	61. 343	1. 00 30. 73
	ATOM	1123	CA	PRO	153	22. 942	6. 248	59. 896	1. 00 34. 59
25	ATOM	1124	CB	PRO	153	22. 397	4. 991	59. 225	1. 00 31. 34
	ATOM	1125	CG	PRO	153	21. 072	4. 812	59. 884	1. 00 31. 98
	ATOM	1126	С	PRO	153	22. 507	7. 535	59. 201	1. 00 37. 30
	ATOM	1127	0	PRO	153	21. 310	7. 813	59.067	1. 00 39. 02
	ATOM	1128	N	VAL	154	23. 483	8. 325	58. 770	1. 00 39. 02

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	ATOM	1129	CA	VAL	154	23. 187	9. 581	58. 092	1. 00 40. 43
	ATOM	1130	CB	VAL	154	23. 446	10. 792	59. 007	1. 00 39. 28
	MOTA	1131	CG	VAL	154	23. 191	12. 081	58. 238	1. 00 41. 18
	ATOM	1132	CG2	VAL	154	22. 557	10. 727	60. 221	1. 00 38. 37
5	ATOM	1133	C	VAL	154	24. 023	9. 785	56. 837	1. 00 41. 48
	ATOM	1134	0	VAL	154	25. 241	9. 602	56. 861	1. 00 41. 28
	ATOM	1135	N	ARG	155	23. 365	10. 162	55. 743	1. 00 43. 31
	ATOM	1136	CA	ARG	155	24. 072	10. 441	54. 495	1. 00 46. 32
	MOTA	1137	CB	ARG	155	23. 233	10. 058	53. 280	1. 00 47. 31
10	ATOM	1138	CG	ARG	155	23. 809	10. 586	51. 968	1. 00 52. 20
	ATOM	1139	CD	ARG	155	23. 563	9. 614	50. 844	1. 00 55. 56
	ATOM	1140	NE	ARG	155	24. 419	8. 437	50. 968	1. 00 59. 93
	ATOM	1141	CZ	ARG	155	24. 068	7. 217	50. 573	1. 00 61. 41
	ATOM	1142	NH1	ARG	155	22. 874	7. 011	50. 032	1. 00 63. 00
15	ATOM	1143	NH2	ARG	155	24. 910	6. 203	50. 717	1. 00 63. 35
	ATOM	1144	C	ARG	155	24. 367	11. 934	54. 456	1. 00 46. 23
	ATOM	1145	0	ARG	155	23. 486	12. 737	54. 166	1. 00 47. 64
	ATOM	1146	N	HIS	156	25. 613	12. 291	54. 754	1. 00 47. 03
	ATOM	1147	CA	HIS	156	26. 046	13. 682	54. 791	1. 00 48. 05
20	ATOM	1148	CB	HIS	156	27. 318	13. 834	55. 632	1. 00 49. 62
	ATOM	1149	CG	HIS	156	27. 157	13. 444	57. 066	1. 00 52. 65
	ATOM	1150	CD2	HIS	156	26. 274	12. 619	57. 676	1. 00 53. 99
	ATOM	1151	ND1	HIS	156	27. 990	13. 916	58. 057	1. 00 53. 35
	ATOM	1152		HIS	156	27. 625	13. 401	59. 218	1. 00 54. 78
25	ATOM	1153	NE2	HIS	156	26. 586	12. 610	59. 014	1. 00 54. 28
	ATOM	1154	C	HIS	156	26. 334	14. 317	53. 440	1. 00 48. 30
	ATOM	1155	0	HIS	156	26. 872	13. 677	52. 535	1. 00 47. 38
	ATOM	1156	N	GLU	157	25. 969	15. 589	53. 319	1. 00 47. 98
	ATOM	1157	CA	GLU	157	26. 256	16. 343	52. 114	1. 00 48. 38

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	ATOM	1158	CB	GLU	157	25. 113	17. 296	51. 749	1. 00 51. 05
	ATOM	1159	CG	GLU	157	25. 462	18. 198	50. 558	1. 00 57. 22
	ATOM	1160	CD	GLU	157	24. 422	19. 276	50. 275	1. 00 58. 92
	ATOM	1161	0E1	GLU	157	23. 299	18. 931	49. 845	1. 00 60. 91
5	ATOM	1162	0E2	GLU	157	24. 734	20. 471	50. 485	1. 00 60. 69
	ATOM	1163	C	GLU	157	27. 475	17. 138	52. 547	1. 00 45. 12
	ATOM	1164	0	GLU	157	28. 349	17. 457	51. 749	1. 00 43. 91
	ATOM	1165	N	ASP	158	27. 529	17. 427	53. 843	1. 00 43. 85
	ATOM	1166	CA	ASP	158	28. 633	18. 174	54. 416	1. 00 43. 81
10	ATOM	1167	CB	ASP	158	28. 479	19. 654	54. 085	1. 00 46. 74
	ATOM	1168	CG	ASP	158	29. 743	20. 445	54. 349	1. 00 49. 54
	MOTA	1169	OD 1	ASP	158	29. 760	21. 651	54. 016	1. 00 53. 34
	ATOM	1170	OD2	ASP	158	30. 716	19. 869	54. 884	1. 00 49. 62
	ATOM	1171	C	ASP	158	28. 671	17. 972	55. 928	1. 00 43. 93
15	ATOM	1172	0	ASP	158	27. 724	17. 447	56. 518	1. 00 43. 97
	ATOM	1173	N	ILE	159	29. 767	18. 399	56. 547	1. 00 43. 75
	ATOM	1174	CA	ILE	159	29. 963	18. 250	57. 983	1. 00 44. 27
	ATOM	1175	CB	ILE	159	31. 248	18. 971	58. 452	1. 00 45. 07
	ATOM	1176	CG2	ILE	159	31. 069	20. 480	58. 354	1. 00 47. 24
20	ATOM	1177	CG1	ILE	159	31. 544	18. 617	59. 907	1. 00 45. 29
	ATOM	1178	CD1	ILE	159	31. 733	17. 140	60. 152	1. 00 48. 99
	ATOM	1179	C	ILE	159	28. 795	18. 744	58. 829	1. 00 44. 47
	ATOM	1180	0	ILE	159	28. 583	18. 254	59. 941	1. 00 44. 15
	ATOM	1181	N .	ASP	160	28. 037	19. 709	58. 317	1. 00 44. 10
25	ATOM	1182	CA A	ASP	160	26. 904	20. 239	59. 072	1. 00 42. 92
	ATOM	1183	CB A	ASP	160	27. 103	21. 734	59. 360	1. 00 44. 13
	ATOM	1184	CG A	ASP	160	27. 448	22. 533	58. 118	1. 00 45. 52
	ATOM	1185	0D1 A	ASP	160	28. 258	23. 479	58. 239	1. 00 47. 57
	ATOM	1186	OD2 A	ASP	160	26. 912	22. 228	57. 031	1. 00 45. 51

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	ATOM	1187	C	ASP	160	25. 559	20. 005	58. 410	1. 00 42. 92
	ATOM	1188	0	ASP	160	24. 579	20. 691	58. 706	1. 00 44. 48
	ATOM	1189	N	LYS	161	25. 509	19. 026	57. 518	1. 00 41. 57
	ATOM	1190	CA	LYS	161	24. 267	18. 692	56. 838	1. 00 41. 51
5	ATOM	1191	CB	LYS	161	24. 067	19. 597	55. 618	1. 00 41. 19
	ATOM	1192	CG	LYS	161	22. 783	19. 306	54. 863	1. 00 41. 39
	ATOM	1193	CD	LYS	161	22. 687	20. 094	53. 557	1. 00 43. 25
	ATOM	1194	CE	LYS	161	21. 366	19. 809	52. 860	1. 00 40. 06
	ATOM	1195	NZ	LYS	161	21. 335	20. 312	51. 468	1. 00 41. 02
10	ATOM	1196	C	LYS	161	24. 258	17. 224	56. 397	1. 00 41. 66
	ATOM	1197	0	LYS	161	25. 239	16. 725	55. 838	1. 00 39. 36
	ATOM	1198	N	GLY	162	23. 143	16. 546	56. 654	1. 00 40. 90
	ATOM	1199	CA	GLY	162	23. 005	15. 152	56. 276	1. 00 42. 70
	ATOM	1200	C	GLY	162	21. 618	14. 645	56. 615	1. 00 43. 15
15	ATOM	1201	0	GLY	162	21.019	15. 085	57. 594	1. 00 43. 59
	ATOM	1202	N	ILE	163	21. 096	13. 722	55. 816	1. 00 43. 93
	ATOM	1203	CA	ILE	163	19. 763	13. 190	56. 068	1. 00 45. 03
	ATOM	1204	CB	ILE	163	18. 958	13. 031	54. 755	1. 00 46. 16
	ATOM	1205	CG2	ILE	163	18. 943	14. 352	53. 985	1. 00 45. 82
20	ATOM	1206	CG1	ILE	163	19. 585	11. 938	53. 889	1. 00 46. 11
	ATOM	1207	CD1	ILE	163	18. 812	11. 638	52. 613	1. 00 48. 51
	ATOM	1208	C	ILE	163	19. 812	11. 833	56. 764	1. 00 46. 49
	ATOM	1209	0	ILE	163	20. 771	11. 074	56. 609	1. 00 45. 36
	ATOM	1210	N	LEU	164	18. 767	11. 545	57. 533	1. 00 47. 21
25	ATOM	1211	CA	LEU	164	18. 649	10. 286	58. 253	1. 00 47. 53
	ATOM	1212	CB	LEU	164	17. 623	10. 414	59. 379	1. 00 47. 11
	ATOM	1213	CG	LEU	164	17. 135	9. 126	60. 049	1. 00 47. 15
	ATOM	1214	CD1		164	18. 265	8. 469	60. 832	1. 00 45. 45
	ATOM	1215	CD2	LEU-	164	15. 981	9. 465	60. 977	1. 00 47. 00

- 58 -ATOM 1216 C LEU 164 18. 189 9. 220 57. 277 1.00 48.06 ATOM 1217 0 LEU 164 17. 137 56.657 9. 352 1. 00 48. 49 ATOM 1218 N LEU 165 18. 977 8. 161 57. 137 1. 00 48. 32 ATOM 1219 CA LEU 165 18. 614 7. 093 56. 224 1.00 47.47 5 ATOM 1220 CBLEU 165 19. 827 6. 208 55. 954 1.00 45.44 ATOM 1221 CG LEU 165 20.867 6. 978 55. 140 1.00 47.60 ATOM 1222 CD1 LEU 165 22. 128 6. 155 54. 956 1.00 47.47 **ATOM** 1223 CD2 LEU 165 20. 261 7. 342 53. 786 1. 00 48. 48 ATOM 1224 C LEU 165 17. 460 6. 300 56. 814 1.00 46.86 ATOM 10 1225 0 LEU 165 16. 497 5. 985 56. 120 1.00 46.90 ATOM 1226 N ASN 166 17. 562 5. 992 58. 101 1.00 46.60 ATOM 1227 CA ASN 166 16. 521 5. 266 58. 817 1. 00 47. 23 ATOM 1228 CBASN 166 16. 282 3. 883 58. 200 1. 00 49. 17 ATOM 1229 CG ASN 166 17. 542 3. 053 58. 118 1. 00 50. 36 15 ATOM 1230 OD1 ASN 166 18. 205 2. 997 57. 076 1. 00 50. 62 ATOM 1231 ND2 ASN 166 17.888 2.406 59. 223 1. 00 50. 50 ATOM 1232 C ASN 166 16. 913 5. 123 60. 279 1.00 47.60 ATOM 1233 0 ASN 166 18.096 5. 177 60. 623 T. 00 48. 53 ATOM 1234 N TRP 167 15.916 4.966 61. 142 1.00 46.96 ATOM 20 1235 CATRP 167 16. 166 4.815 62. 571 1. 00 45. 46 ATOM 1236 CBTRP 167 14. 890 5. 085 63. 376 1. 00 47. 63 ATOM 1237 CG TRP 167 14. 433 6. 519 63. 454 1. 00 49. 15 ATOM 1238 CD2 TRP 167 15.093 7.602 64. 126 1. 00 49. 07 ATOM 1239 CE2 TRP 167 14. 237 8. 725 64.050 1. 00 48. 21 25 **ATOM** 1240 CE3 TRP 167 16. 321 7. 732 64. 787 1. 00 49. 17 ATOM 1241 CD1 TRP 167 13. 242 7. 022 63.003 1. 00 49. 03 ATOM 1242 NE1 TRP 167 13. 117 8. 343 63. 361 1. 00 48. 46 ATOM CZ2 TRP 1243 167 14. 569 9. 962 64. 614 1. 00 47. 68

ATOM

1244

CZ3 TRP

167

16. 652

8. 966

65. 348

1. 00 49. 58

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						0.0	,				
	ATOM	1245	CH2	2 TRP	167	15. 777	10. 064	65. 256	1. 00	48. 80	
	ATOM	1246	C	TRP	167	16. 647	3. 394	62. 890	1. 00	43. 28	
	ATOM	1247	0	TRP	167	16. 425	2. 461	62. 119	1. 00	42. 86	
	ATOM	1248	N	THR	168	17. 297	3. 245	64. 038	1. 00	41. 63	
5	ATOM	1249	CA	THR	168	17. 796	1. 953	64. 501	1. 00	40. 13	
	ATOM	1250	CB	THR	168	19. 275	1. 723	64. 086	1. 00	37. 87	
	ATOM	1251	0G1	THR	168	20. 082	2. 795	64. 587	1. 00	33. 52	
	ATOM	1252	CG2	THR	168	19. 417	1. 647	62. 566	1. 00	34. 11	
	ATOM	1253	C	THR	168	17. 719	1. 943	66. 029	1. 00	41. 33	
10	ATOM	1254	0	THR	168	17. 382	2. 953	66. 649	1. 00	41. 41	
	ATOM	1255	N	LYS	169	18. 025	0. 799	66. 631	1. 00	42. 06	
	ATOM	1256	CA	LYS	169	18. 013	0. 672	68. 083	1. 00	42. 59	
	ATOM	1257	CB	LYS	169	19. 077	1. 594	68. 683	1. 00	39. 56	
	ATOM	1258	CG	LYS	169	20. 497	1. 209	68. 287	1. 00	36. 24	
15	ATOM	1259	CD	LYS	169	21. 528	2. 170	68. 840	1. 00	33. 26	
	ATOM	1260	CE	LYS	169	21. 481	3. 514	68. 133	1. 00	30. 26	
	ATOM	1261	NZ	LYS	169	22. 589	4. 373	68. 610	1. 00	32. 75	
	ATOM	1262	C	LYS	169	16.661	0. 933	68. 751	1. 00	45. 26	
	ATOM	1263	0	LYS	169	16. 598	1. 191	69. 955	1. 00	45. 85	
20	ATOM	1264	N	GLY	170	15. 583	0. 881	67. 975	1. 00	47. 46	
	ATOM	1265	CA	GLY	170	14. 267	1. 083	68. 555	1. 00	52. 44	
	ATOM	1266	C	GLY	170	13. 552	2. 394	68. 295	1. 00	55. 24	
	ATOM	1267	0	GLY	170	12. 324	2. 422	68. 275	1. 00	56. 11	
	ATOM	1268	N	PHE	171	14. 293	3. 482	68. 118	1. 00	58. 10	
25	ATOM	1269	CA	PHE	171	13. 668	4. 777	67. 861	1. 00	61.86	
	ATOM	1270	CB	PHE	171	14. 734	5. 846	67. 613	1. 00	62. 35	
	ATOM	1271	CG	PHE	171	15. 449	6. 285	68. 856	1. 00	64. 08	
	ATOM	1272	CD1	PHE	171	16. 060	5. 354	69. 691	1. 00	66. 00	
	ATOM	1273	CD2	PHE	171	15. 511	7. 630	69. 196	1. 00	64. 53	

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	ATOM	1274	CE	1 PHE	171	16. 721	5. 760	70. 851	1. 00 66. 96
	ATOM	1275	CE	2 PHE	171	16. 170	8. 046	70. 352	1. 00 65. 93
	ATOM	1276	CZ	PHE	171	16. 776	7. 109	71. 180	1. 00 66. 07
	ATOM	1277	C	PHE	171	12. 727	4. 697	66. 663	1. 00 63. 91
5	ATOM	1278	0	PHE	171	12. 994	3. 975	65. 702	1. 00 63. 50
	ATOM	1279	N	LYS	172	11. 620	5. 430	66. 727	1. 00 65. 77
	ATOM	1280	CA	LYS	172	10. 657	5. 424	65. 633	1. 00 68. 37
	ATOM	1281	CB	LYS	172	9. 738	4. 197	65. 727	1. 00 70. 16
	ATOM	1282	CG	LYS	172	8. 814	4. 035	64. 517	1. 00 72. 04
10	ATOM	1283	CD	LYS	172	7. 867	2. 842	64. 647	1. 00 73. 43
	ATOM	1284	CE	LYS	172	6. 977	2. 718	63. 406	1. 00 74. 42
	ATOM	1285	NZ	LYS	172	5. 933	1. 655	63. 525	1. 00 73. 62
	ATOM	1286	C	LYS	172	9. 808	6. 688	65. 606	1. 00 69. 18
	ATOM	1287	0	LYS	172	8. 599	6. 642	65. 838	1. 00 70. 01
15	ATOM	1288	N	ALA	173	10. 445	7. 820	65. 332	1. 00 68. 98
	ATOM	1289	CA	ALA	173	9. 734	9. 086	65. 251	1. 00 69. 07
	ATOM	1290	СВ	ALA	173	10. 598	10. 210	65. 818	1. 00 68. 41
	ATOM	1291	C	ALA	173	9. 424	9. 339	63. 776	1. 00 69. 07
	ATOM	1292	0	ALA	173	10. 336	9. 471	62. 962	1. 00 69. 61
20	ATOM	1293	N	SER	174	8. 139	9. 394	63. 432	1. 00 69. 06
	ATOM	1294	CA	SER	174	7. 735	9. 620	62. 047	1. 00 68. 32
	ATOM	1295	CB	SER	174	6. 217	9. 491	61. 901	1. 00 69. 02
	ATOM	1296	0G	SER	174	5. 546	10. 503	62. 632	1. 00 68. 18
	ATOM	1297	C	SER	174	8. 173	10. 996	61. 568	1. 00 67. 71
25	ATOM	1298	0	SER	174	8. 410	11. 897	62. 370	1. 00 68. 23
	ATOM	1299	N	GLY	175	8. 288	11. 148	60. 254	1. 00 67. 37
	ATOM	1300	CA	GLY	175	8. 688	12. 424	59. 690	1. 00 67. 08
	ATOM	1301	С	GLY	175	10. 143	12. 787	59. 915	1. 00 66. 86
	ATOM	1302	0	GLY	175	10. 507	13. 962	59. 855	1. 00 67. 38

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	ATOM	1303	N	ALA	176	10. 979	11. 786	60. 172	1. 00 66. 42
	ATOM	1304	CA	ALA	176	12. 400	12. 018	60. 401	1. 00 64. 67
	ATOM	1305	CB	ALA	176	12. 828	11. 360	61. 699	1. 00 64. 11
	ATOM	1306	C	ALA	176	13. 229	11. 475	59. 242	1. 00 64. 02
5	ATOM	1307	0	ALA	176	14. 053	12. 183	58. 667	1. 00 65. 00
	ATOM	1308	N	GLU	177	12. 993	10. 214	58. 903	1. 00 63. 24
	ATOM	1309	CA	GLU	177	13. 710	9. 544	57. 825	1. 00 63. 08
	ATOM	1310	CB	GLU	177	13. 147	8. 127	57. 639	1. 00 62. 97
	ATOM	1311	CG	GLU	177	13. 315	7. 224	58. 865	1. 00 64. 81
10	ATOM	1312	CD	GLU	177	12. 712	5. 837	58. 682	1. 00 64. 99
	ATOM	1313	0E1	GLU	177	12. 948	4. 972	59. 552	1. 00 65. 80
	ATOM	1314	0E2	GLU	177	12. 003	5. 612	57. 677	1. 00 64. 52
	ATOM	1315	C	GLU	177	13. 669	10. 293	56. 491	1. 00 62. 92
	ATOM	1316	0	GLU	177	12. 602	10. 489	55. 908	1. 00 63. 26
15	ATOM	1317	N	GLY	178	14. 838	10. 708	56. 013	1. 00 62. 46
	ATOM	1318	CA	GLY	178	14. 911	11. 406	54. 741	1. 00 61. 36
	ATOM	1319	C	GLY	178	15. 095	12. 911	54. 805	1. 00 60. 52
	ATOM	1320	0	GLY	178	15. 337	13. 539	53. 777	1. 00 61. 73
	ATOM	1321	N	ASN	179	14. 990	13. 498	55. 993	1. 00 59. 84
20	ATOM	1322	CA	ASN	179	15. 139	14. 942	56. 134	1. 00 59. 11
	ATOM	1323	CB	ASN	179	13. 985	15. 512	56. 959	1. 00 59. 72
	ATOM	1324	CG	ASN	179	12. 630	15. 217	56. 342	1. 00 61. 46
	ATOM	1325	OD1	ASN	179	12. 423	15. 416	55. 143	1. 00 61. 86
	ATOM	1326	ND2	ASN	179	11. 696	14. 743	57. 161	1. 00 61. 02
25	ATOM	1327	C	ASN	179	16. 463	15. 349	56. 765	1. 00 58. 81
	ATOM	1328	0	ASN	179	17. 108	14. 553	57. 441	1. 00 59. 10
	ATOM	1329	N	ASN	180	16. 860	16. 599	56. 537	1. 00 58. 30
	ATOM	1330	CA	ASN	180	18. 107	17. 130	57. 079	1. 00 57. 96
	ATOM	1331	CB	ASN	180	18. 362	18. 539	56. 539	1. 00 58. 57

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	ATOM	1332	CG	ASN	180	19. 693	19. 112	57. 001	1. 00 60. 99
	ATOM	1333	OD 1	ASN	180	20. 278	18. 647	57. 983	1. 00 60. 88
	ATOM	1334	ND2	ASN	180	20. 171	20. 139	56. 302	1. 00 60. 74
	ATOM	1335	C	ASN	180	18. 036	17. 183	58. 600	1. 00 57. 30
5	ATOM	1336	0	ASN	180	17. 388	18. 064	59. 162	1. 00 57. 94
	ATOM	1337	N	VAL	181	18. 709	16. 245	59. 261	1. 00 55. 49
	ATOM	1338	CA	VAL	181	18. 716	16. 189	60. 720	1. 00 54. 19
	ATOM	1339	CB	VAL	181	19. 698	15. 109	61. 229	1. 00 53. 15
	ATOM	1340	CG1	VAL	181	19. 756	15. 121	62. 748	1. 00 50. 90
10	ATOM	1341	CG2	VAL	181	19. 258	13. 742	60. 731	1. 00 51. 33
	ATOM	1342	C	VAL	181	19. 089	17. 534	61. 333	1. 00 54. 31
	ATOM	1343	0	VAL	181	18. 473	17. 979	62. 299	1. 00 53. 21
	ATOM	1344	N	VAL	182	20. 110	18. 174	60. 777	1. 00 56. 27
	ATOM	1345	CA	VAL	182	20. 533	19. 472	61. 271	1. 00 58. 32
15	ATOM	1346	CB	VAL	182	21. 706	20. 033	60. 447	1. 00 58. 42
	ATOM	1347	CG1	VAL	182	22. 135	21. 373	61. 007	1. 00 58. 05
	ATOM	1348	CG2	VAL	182	22. 867	19. 054	60. 460	1. 00 59. 02
	ATOM	1349	C	VAL	182	19. 339	20. 410	61. 125	1. 00 60. 16
	ATOM	1350	0	VAL	182	19. 052	21. 220	62. 008	1. 00 59. 87
20	ATOM	1351	N	GLY	183	18. 640	20. 275	60. 003	1. 00 61. 05
	ATOM	1352	CA	GLY	183	17. 480	21. 103	59. 741	1. 00 63. 47
	ATOM	1353	C	GLY	183	16. 412	20. 967	60. 805	1. 00 64. 68
	ATOM	1354	0	GLY	183	15. 873	21. 966	61. 280	1. 00 64. 59
	ATOM	1355	N	LEU	184	16. 103	19. 733	61. 187	1. 00 65. 39
25	ATOM	1356	CA	LEU	184	15. 091	19. 502	62. 203	1. 00 66. 47
	ATOM	1357	CB	LEU	184	14. 855	18. 005	62. 387	1. 00 66. 17
	ATOM	1358	CG	LEU	184	14. 407	17. 254	61. 132	1. 00 67. 51
	ATOM	1359	CD1	LEU	184	14. 116	15. 805	61. 486	1. 00 66. 63
	ATOM	1360	CD2	LEU	184	13. 168	17. 913	60. 546	1. 00 68. 22

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	ATOM	1361	C	LEU	184	15. 502	20. 130	63. 528	1. 00 67. 67
	ATOM	1362	0	LEU	184	14. 651	20. 570	64. 301	1. 00 68. 91
	ATOM	1363	N	LEU	185	16. 804	20. 176	63. 790	1. 00 68. 11
	ATOM	1364	CA	LEU	185	17. 297	20. 759	65. 031	1. 00 68. 91
5	ATOM	1365	CB	LEU	185	18. 797	20. 501	65. 194	1. 00 67. 32
	ATOM	1366	CG	LEU	185	19. 409	21. 060	66. 482	1. 00 66. 21
	ATOM	1367	CD	1 LEU	185	18. 776	20. 375	67. 676	1. 00 65. 16
	ATOM	1368	CD	2 LEU	185	20. 913	20. 851	66. 486	1. 00 66. 43
	ATOM	1369	C	LEU	185	17. 034	22. 262	65. 058	1. 00 70. 10
10	ATOM	1370	0	LEU	185	16. 422	22. 776	65. 991	1. 00 70. 26
	ATOM	1371	N	ARG	186	17. 505	22. 962	64. 033	1. 00 71. 83
	ATOM	1372	CA	ARG	186	17. 314	24. 403	63. 948	1. 00 73. 78
	ATOM	1373	CB	ARG	186	18. 015	24. 941	62. 700	1. 00 73. 97
	ATOM	1374	CG	ARG	186	19. 533	24. 881	62. 804	1. 00 74. 09
15	ATOM	1375	CD	ARG	186	20. 206	24. 984	61. 448	1. 00 74. 37
	ATOM	1376	NE	ARG	186	21. 662	24. 945	61. 571	1. 00 75. 77
	ATOM	1377	CZ	ARG	186	22. 503	24. 860	60. 543	1. 00 75. 94
	ATOM	1378	NH 1	ARG	186	22. 036	24. 800	59. 303	1. 00 75. 97
	ATOM	1379	NH2	ARG	186	23. 815	24. 841	60. 755	1. 00 75. 99
20	ATOM	1380	C	ARG	186	15. 825	24. 737	63. 927	1. 00 74. 93
	ATOM	1381	0	ARG	186	15. 365	25. 609	64. 665	1. 00 74. 59
	ATOM	1382	N	ASP	187	15. 074	24. 023	63. 095	1. 00 76. 23
	ATOM	1383	CA	ASP	187	13. 632	24. 225	62. 981	1. 00 77. 59
	ATOM	1384	CB	ASP	187	13. 018	23. 128	62. 102	1. 00 75. 83
25	ATOM	1385	CG	ASP	187	13. 203	23. 391	60. 614	1. 00 74. 87
	ATOM	1386	OD1	ASP	187	14. 193	24. 051	60. 234	1. 00 73. 64
	ATOM	1387	OD2	ASP	187	12. 359	22. 924	59. 820	1. 00 74. 33
	ATOM	1388	C	ASP	187	12. 945	24. 236	64. 349	1. 00 79. 78
	ATOM	1389	0	ASP	187	11. 963	24. 952	64. 551	1. 00 80. 50

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ATOM 1391 CA ALA 188 12.883 23.379 66.625 1.00 82 ATOM 1392 CB ALA 188 13.118 22.000 67.230 1.00 83 ATOM 1393 C ALA 188 13.477 24.456 67.525 1.00 84 5 ATOM 1394 O ALA 188 12.783 25.019 68.376 1.00 84 ATOM 1395 N ILE 189 14.763 24.736 67.338 1.00 85 ATOM 1396 CA ILE 189 15.445 25.753 68.127 1.00 86 ATOM 1397 CB ILE 189 16.947 25.819 67.776 1.00 86 ATOM 1398 CG2 ILE 189 17.585 27.049 68.409 1.00 85 ATOM 1399 CG1 ILE 189 17.641 24.541 68.253 1.00 86. ATOM 1400 CD1 ILE 189 19.136 24.516 68.004 1.00 86. ATOM 1401 C ILE 189 14.812 27.114 67.871 1.00 88. ATOM 1402 O ILE 189 14.812 27.114 67.871 1.00 88. ATOM 1403 N LYS 190 14.278 27.295 66.666 1.00 90. 15 ATOM 1404 CA LYS 190 13.638 28.551 66.291 1.00 91. ATOM 1405 CB LYS 190 13.678 28.729 64.770 1.00 92. ATOM 1406 CG LYS 190 15.032 29.205 64.234 1.00 93.	10 13 33 87 40 37 52 36 85 64 36
ATOM 1392 CB ALA 188 13. 118 22. 000 67. 230 1. 00 83 ATOM 1393 C ALA 188 13. 477 24. 456 67. 525 1. 00 84 5 ATOM 1394 O ALA 188 12. 783 25. 019 68. 376 1. 00 84 ATOM 1395 N ILE 189 14. 763 24. 736 67. 338 1. 00 85 ATOM 1396 CA ILE 189 15. 445 25. 753 68. 127 1. 00 86 ATOM 1397 CB ILE 189 16. 947 25. 819 67. 776 1. 00 86 ATOM 1398 CG2 ILE 189 17. 585 27. 049 68. 409 1. 00 85 ATOM 1399 CG1 ILE 189 17. 641 24. 541 68. 253 1. 00 86. ATOM 1400 CD1 ILE 189 19. 136 24. 516 68. 004 1. 00 86. ATOM 1401 C ILE 189 14. 812 27. 114 67. 871 1. 00 88. ATOM 1402 O ILE 189 14. 802 27. 978 68. 748 1. 00 89. ATOM 1403 N LYS 190 14. 278 27. 295 66. 666 1. 00 90. 15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	10 13 33 87 40 37 52 36 85 64 36
5 ATOM 1394 O ALA 188 12. 783 25. 019 68. 376 1. 00 84 ATOM 1395 N ILE 189 14. 763 24. 736 67. 338 1. 00 85 ATOM 1396 CA ILE 189 15. 445 25. 753 68. 127 1. 00 86 ATOM 1397 CB ILE 189 16. 947 25. 819 67. 776 1. 00 86 ATOM 1398 CG2 ILE 189 17. 585 27. 049 68. 409 1. 00 85. ATOM 1399 CG1 ILE 189 17. 641 24. 541 68. 253 1. 00 86. ATOM 1400 CD1 ILE 189 19. 136 24. 516 68. 004 1. 00 86. ATOM 1401 C ILE 189 14. 812 27. 114 67. 871 1. 00 88. ATOM 1402 O ILE 189 14. 802 27. 978 68. 748 1. 00 89. ATOM 1403 N LYS 190 14. 278 27. 295 66. 666 1. 00 90. 15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	10 33 87 40 37 52 36 85 64 36
5 ATOM 1394 0 ALA 188 12.783 25.019 68.376 1.00 84 ATOM 1395 N ILE 189 14.763 24.736 67.338 1.00 85 ATOM 1396 CA ILE 189 15.445 25.753 68.127 1.00 86 ATOM 1397 CB ILE 189 16.947 25.819 67.776 1.00 86 ATOM 1398 CG2 ILE 189 17.585 27.049 68.409 1.00 85 ATOM 1399 CG1 ILE 189 17.641 24.541 68.253 1.00 86 ATOM 1400 CD1 ILE 189 19.136 24.516 68.004 1.00 86 ATOM 1401 C ILE 189 14.812 27.114 67.871 1.00 88 ATOM 1402 O ILE 189 14.802 27.978 68.748 1.00 90 15 ATOM 1404 CA LYS 190 13.638 28.729 64.77	10 33 87 40 37 52 36 85 64 36
ATOM 1396 CA ILE 189 15. 445 25. 753 68. 127 1. 00 86 ATOM 1397 CB ILE 189 16. 947 25. 819 67. 776 1. 00 86 ATOM 1398 CG2 ILE 189 17. 585 27. 049 68. 409 1. 00 85. 10 ATOM 1399 CG1 ILE 189 17. 641 24. 541 68. 253 1. 00 86. ATOM 1400 CD1 ILE 189 19. 136 24. 516 68. 004 1. 00 86. ATOM 1401 C ILE 189 14. 812 27. 114 67. 871 1. 00 88. ATOM 1402 0 ILE 189 14. 802 27. 978 68. 748 1. 00 89. ATOM 1403 N LYS 190 14. 278 27. 295 66. 666 1. 00 90. 15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	87 40 37 52 36 85 64 36
ATOM 1397 CB ILE 189 16. 947 25. 819 67. 776 1. 00 86 ATOM 1398 CG2 ILE 189 17. 585 27. 049 68. 409 1. 00 85. 10 ATOM 1399 CG1 ILE 189 17. 641 24. 541 68. 253 1. 00 86. ATOM 1400 CD1 ILE 189 19. 136 24. 516 68. 004 1. 00 86. ATOM 1401 C ILE 189 14. 812 27. 114 67. 871 1. 00 88. ATOM 1402 O ILE 189 14. 802 27. 978 68. 748 1. 00 89. ATOM 1403 N LYS 190 14. 278 27. 295 66. 666 1. 00 90. 15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	40 37 52 36 85 64 36
ATOM 1398 CG2 ILE 189 17. 585 27. 049 68. 409 1. 00 85. 10 ATOM 1399 CG1 ILE 189 17. 641 24. 541 68. 253 1. 00 86. ATOM 1400 CD1 ILE 189 19. 136 24. 516 68. 004 1. 00 86. ATOM 1401 C ILE 189 14. 812 27. 114 67. 871 1. 00 88. ATOM 1402 O ILE 189 14. 802 27. 978 68. 748 1. 00 89. ATOM 1403 N LYS 190 14. 278 27. 295 66. 666 1. 00 90. 15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	37 52 36 85 64 36
10 ATOM 1399 CG1 ILE 189 17. 641 24. 541 68. 253 1. 00 86. ATOM 1400 CD1 ILE 189 19. 136 24. 516 68. 004 1. 00 86. ATOM 1401 C ILE 189 14. 812 27. 114 67. 871 1. 00 88. ATOM 1402 0 ILE 189 14. 802 27. 978 68. 748 1. 00 89. ATOM 1403 N LYS 190 14. 278 27. 295 66. 666 1. 00 90. 15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	52 36 85 64 36
ATOM 1400 CD1 ILE 189 19. 136 24. 516 68. 004 1. 00 86. ATOM 1401 C ILE 189 14. 812 27. 114 67. 871 1. 00 88. ATOM 1402 O ILE 189 14. 802 27. 978 68. 748 1. 00 89. ATOM 1403 N LYS 190 14. 278 27. 295 66. 666 1. 00 90. 15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	36 85 64 36
ATOM 1401 C ILE 189 14. 812 27. 114 67. 871 1. 00 88. ATOM 1402 0 ILE 189 14. 802 27. 978 68. 748 1. 00 89. ATOM 1403 N LYS 190 14. 278 27. 295 66. 666 1. 00 90. 15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	85 64 36
ATOM 1402 0 ILE 189 14. 802 27. 978 68. 748 1. 00 89. ATOM 1403 N LYS 190 14. 278 27. 295 66. 666 1. 00 90. 15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	64 36
ATOM 1403 N LYS 190 14. 278 27. 295 66. 666 1. 00 90. 15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	36
15 ATOM 1404 CA LYS 190 13. 638 28. 551 66. 291 1. 00 91. ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	
ATOM 1405 CB LYS 190 13. 678 28. 729 64. 770 1. 00 92.	
ATOM 1406 CC LVC 100 15 000 00 007.	75
ATOM 1406 CG LYS 190 15.032 29.205 64.234 1.00 93.	26
	56
ATOM 1407 CD LYS 190 16.174 28.282 64.652 1.00 94.	17
ATOM 1408 CE LYS 190 17.507 28.722 64.064 1.00 94.	42
20 ATOM 1409 NZ LYS 190 18.605 27.773 64.409 1.00 93.	91
ATOM 1410 C LYS 190 12. 202 28. 645 66. 803 1. 00 92.	34
ATOM 1411 0 LYS 190 11.612 29.723 66.817 1.00 92.	32
ATOM 1412 N ARG 191 11.639 27.516 67.221 1.00 92.	78
ATOM 1413 CA ARG 191 10.286 27.502 67.763 1.00 93.	11
25 ATOM 1414 CB ARG 191 9.674 26.108 67.658 1.00 93.	7
ATOM 1415 CG ARG 191 9.711 25.497 66.275 1.00 93.	6
ATOM 1416 CD ARG 191 9.530 23.993 66.378 1.00 93.	1
ATOM 1417 NE ARG 191 9.816 23.310 65.123 1.00 93.9	9
ATOM 1418 CZ ARG 191 10.012 22.000 65.017 1.00 94.	

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	ATOM	1419	NH	11 ARG	191	9. 954	21. 231	66. 095	1. 00 94. 65
	ATOM	1420	NH	2 ARG	191	10. 269	21. 459	63. 835	1. 00 94. 96
	ATOM	1421	C	ARG	191	10. 432	27. 866		1. 00 94. 00
	ATOM	1422	0	ARG	191	9. 526	27. 654		
5	ATOM	1423	N	ARG	192	11. 596	28. 408	69. 574	1. 00 94. 91
	ATOM	1424	CA	ARG	192	11. 897	28. 795	70. 943	1. 00 96. 15
	ATOM	1425	СВ	ARG	192	13. 049	27. 944	71. 482	1. 00 96. 57
	ATOM	1426	CG	ARG	192	12. 733	26. 469	71. 581	
	ATOM	1427	CD	ARG	192	11. 737	26. 209	72. 689	
10	ATOM	1428	NE	ARG	192	11. 339	24. 808	72. 745	1. 00 98. 97
	ATOM	1429	CZ	ARG	192	10. 624	24. 278	73. 730	1. 00 99. 63
	ATOM	1430	NH	l ARG	192	10. 230	25. 035	74. 746	1. 00 99. 17
	ATOM	1431	NH2	2 ARG	192	10. 300	22. 992	73. 700	1. 00 99. 97
	ATOM	1432	C	ARG	192	12. 273	30. 265	71. 062	1. 00 96. 50
15	ATOM	1433	0	ARG	192	11. 603	31. 035	71. 752	1. 00 96. 60
	ATOM	1434	N	GLY	193	13. 352	30. 652	70. 386	1. 00 96. 89
	ATOM	1435	CA	GLY	193	13. 812	32. 026	70. 465	1. 00 97. 08
	ATOM	1436	C	GLY	193	14. 385	32. 217	71. 855	1. 00 97. 08
	ATOM	1437	0	GLY	193	15. 060	33. 204	72. 147	1. 00 96. 46
20	ATOM	1438	N	ASP	194	14. 104	31. 235	72. 707	1. 00 97. 36
	ATOM	1439	CA	ASP	194	14. 552	31. 205	74. 092	1. 00 97. 35
	ATOM	1440	CB	ASP	194	13. 938	29. 984	74. 789	1. 00 98. 43
	ATOM	1441	CG	ASP	194	13. 764	30. 181	76. 284	1. 00 99. 62
	ATOM	1442	OD 1	ASP	194	13. 117	31. 173	76. 683	1. 00100. 29
25	MOTA	1443	OD2	ASP	194	14. 262	29. 338	77. 059	1. 00 99. 87
	ATOM	1444	C	ASP	194	16. 078	31. 122	74. 122	1. 00 96. 90
	ATOM	1445	0	ASP	194	16. 715	31. 471	75. 118	1. 00 97. 50
	ATOM	1446	N	PHE	195	16. 657	30. 655	73. 018	1. 00 95. 62
	ATOM	1447	CA	PHE	195	18. 105	30. 524	72. 896	1. 00 94. 15

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	ATOM	1448	CB	PHE	195	18. 598	29. 309	73. 697	1. 00 94. 86
	ATOM	1449	CG	PHE	195	18. 043	27. 988	73. 224	1. 00 95. 10
	ATOM	1450	CD	1 PHE	195	18. 560	27. 360	72. 095	1. 00 95. 09
	ATOM	1451	CD	2 PHE	195	17. 005	27. 369	73. 916	1. 00 95. 17
5	ATOM	1452	CE	1 PHE	195	18. 053	26. 136	71. 663	1. 00 95. 14
	ATOM	1453	CE	2 PHE	195	16. 491	26. 145	73. 492	1. 00 95. 12
	ATOM	1454	CZ	PHE	195	17. 016	25. 528	72. 364	1. 00 94. 97
	ATOM	1455	C	PHE	195	18. 508	30. 393	71. 430	1. 00 92. 64
	ATOM	1456	0	PHE	195	17. 667	30. 131	70. 569	1. 00 92. 22
10	ATOM	1457	N	GLU	196	19. 793	30. 583	71. 148	1. 00 90. 93
	ATOM	1458	CA	GLU	196	20. 292	30. 486	69. 779	1. 00 89. 04
	ATOM	1459	CB	GLU	196	20. 249	31. 861	69. 102	1. 00 89. 55
	ATOM	1460	CG	GLU	196	18. 846	32. 395	68. 832	1. 00 90. 25
	ATOM	1461	CD	GLU	196	18. 859	33. 771	68. 187	1. 00 90. 61
15	ATOM	1462	0E1	GLU	196	19. 342	34. 728	68. 830	1. 00 90. 30
	ATOM	1463	0E2	GLU	196	18. 390	33. 895	67. 035	1. 00 90. 79
	ATOM	1464	C	GLU	196	21. 711	29. 923	69. 694	1. 00 87. 11
	ATOM	1465	0	GLU	196	22. 681	30. 589	70. 066	1. 00 86. 83
	ATOM	1466	N	MET	197	21. 824	28. 692	69. 201	1. 00 84. 23
20	ATOM	1467	CA	MET	197	23. 121	28. 043	69. 045	1. 00 80. 79
	ATOM	1468	CB	MET	197	23. 067	26. 586	69. 524	1. 00 81. 16
	ATOM	1469	CG	MET	197	22. 633	26. 389	70. 967	1. 00 80. 14
	ATOM	1470	SD	MET	197	23. 597	27. 356	72. 135	1. 00 81. 93
	ATOM	1471	CE	MET	197	25. 195	26. 640	71. 968	1. 00 81. 72
25	ATOM	1472	C	MET	197	23. 502	28. 070	67. 568	1. 00 77. 74
	ATOM	1473	0	MET	197	22. 695	28. 436	66. 716	1. 00 76. 30
	ATOM	1474	N	ASP	198	24. 733	27. 672	67. 269	1. 00 75. 73
	ATOM	1475	CA	ASP	198	25. 214	27. 652	65. 894	1. 00 72. 50
	ATOM	1476	CB	ASP	198	26. 297	28. 723	65. 720	1. 00 73. 47

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	ATOM	1477	CG	ASP	198	26. 573	29. 046	64. 265	1. 00 75. 34
	ATOM	1478	OD	1 ASP	198				1. 00 75. 72
	ATOM	1479	OD	2 ASP	198	25. 954	28. 407	63. 384	1. 00 76. 53
	ATOM	1480	C	ASP	198	25. 769	26. 265	65. 544	1. 00 69. 75
5	ATOM	1481	0	ASP	198	26. 962	26. 005	65., 703	1. 00 69. 48
	ATOM	1482	N	VAL	199	24. 892	25. 383	65. 068	1. 00 66. 43
	ATOM	1483	CA	VAL	199	25. 266	24. 018	64. 697	1. 00 62. 47
	ATOM	1484	CB	VAL	199	24. 055	23. 266	64. 113	1. 00 62. 19
	ATOM	1485	CG	l VAL	199	24. 426	21. 823	63. 827	1. 00 61. 88
10	ATOM	1486	CG	2 VAL	199	22. 886	23. 340	65. 083	1. 00 61. 21
	ATOM	1487	C	VAL	199	26. 409	23. 986	63. 682	1. 00 60. 44
	ATOM	1488	0	VAL	199	26. 192	24. 135	62. 479	1. 00 59. 37
	ATOM	1489	N	VAL	200	27. 624	23. 774	64. 180	1. 00 58. 00
	ATOM	1490	CA	VAL	200	28. 820	23. 741	63. 341	1. 00 56. 24
15	ATOM	1491	CB	VAL	200	30. 048	24. 278	64. 128	1. 00 57. 42
	ATOM	1492	CG1	VAL	200	31. 326	24. 071	63. 331	1. 00 57. 94
	ATOM	1493	CG2	VAL	200	29. 859	25. 761	64. 433	1. 00 59. 29
	ATOM	1494	C	VAL	200	29. 159	22. 357	62. 785	1. 00 54. 53
	ATOM	1495	0	VAL	200	29. 759	22. 242	61. 715	1. 00 54. 29
20	ATOM	1496	N	ALA	201	28. 779	21. 306	63. 503	1. 00 52. 88
	ATOM	1497	CA	ALA	201	29. 085	19. 953	63. 048	1. 00 49. 83
	ATOM	1498	CB	ALA	201	30. 541	19. 627	63. 349	1. 00 47. 49
	ATOM	1499	С	ALA	201	28. 196	18. 887	63. 654	1. 00 46. 62
	ATOM	1500	0	ALA	201	27. 803	18. 973	64. 810	1. 00 47. 96
25	ATOM	1501	N	MET	202	27. 873	17. 883	62. 851	1. 00 44. 82
	ATOM	1502	CA	MET	202	27. 065	16. 762	63. 309	1. 00 42. 12
	ATOM	1503	CB	MET	202	25. 731	16. 695	62. 567	1. 00 39. 23
	ATOM	1504	CG	MET	202	24. 886	15. 520	63. 014	1. 00 38. 13
	ATOM	1505	SD	MET	202	23. 425	15. 193	62. 026	1. 00 40. 98

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	ATOM	1506	CE	MET	202	24. 134	15. 162	60. 401	1. 00 37. 63
	ATOM	1507	C	MET	202	27. 865	15. 489	63. 027	1. 00 40. 68
	ATOM	1508	0	MET	202	28. 274	15. 251	61. 888	1. 00 38. 74
	ATOM	1509	N	VAL	203	28. 092	14. 679	64. 060	1. 00 39. 90
5	ATOM	1510	CA	VAL	203	28. 851	13. 438	63. 901	1. 00 37. 47
	ATOM	1511	CB	VAL	203	30. 264	13. 549	64. 517	1. 00 36. 73
	ATOM	1512	CG1	VAL	203	31. 078	14. 615	63. 796	1. 00 34. 96
	ATOM	1513	CG2	VAL	203	30. 155	13. 852	65. 996	1. 00 37. 90
	ATOM	1514	C	VAL	203	28. 190	12. 199	64. 505	1. 00 37. 09
10	ATOM	1515	0	VAL	203	27. 250	12. 284	65. 309	1. 00 36. 61
	ATOM	1516	N	ASN	204	28. 707	11. 039	64. 101	1. 00 36. 09
	ATOM	1517	CA	ASN	204	28. 228	9. 749	64. 584	1. 00 31. 60
	ATOM	1518	CB	ASN	204	28. 461	8. 695	63. 497	1. 00 32. 07
	ATOM	1519	CG	ASN	204	27. 949	7. 322	63. 888	1. 00 31. 63
15	ATOM	1520	0D1	ASN	204	28. 729	6. 443	64. 250	1. 00 30. 91
	ATOM	1521	ND2	ASN	204	26. 634	7. 135	63. 824	1. 00 28. 99
	ATOM	1522	C	ASN	204	29. 027	9. 454	65. 853	1. 00 28. 81
	ATOM	1523	0	ASN	204	30. 122	9. 990	66. 019	1. 00 30. 24
	ATOM	1524	N	ASP	205	28. 498	8. 639	66. 765	1. 00 27. 90
20	ATOM	1525	CA	ASP	205	29. 240	8. 361	67. 995	1. 00 26. 70
	ATOM	1526	CB	ASP	205	28. 369	7. 627	69. 028	1. 00 27. 65
	ATOM	1527	CG	ASP	205	27. 642	6. 438	68. 455	1. 00 30. 26
	ATOM	1528	OD1	ASP	205	27. 079	5. 655	69. 256	1. 00 28. 60
	ATOM	1529	OD2	ASP	205	27. 623	6. 289	67. 213	1. 00 31. 99
25	ATOM	1530	C	ASP	205	30. 573	7. 630	67. 791	1. 00 26. 87
	ATOM	1531	0	ASP	205	31. 498	7. 810	68. 581	1. 00 27. 79
	ATOM	1532	N	THR	206	30. 686	6. 816	66. 740	1. 00 24. 79
	ATOM	1533	CA	THR	206	31. 951	6. 146	66. 476	1. 00 24. 03
	ATOM	1534	CB	THR	206	31. 886	5. 236	65. 206	1. 00 25. 43

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	ATOM	1535	0G	1 THR	206	31. 401	5. 999	64. 089	1. 00 26. 30
	ATOM	1536	CG	2 THR	206	30. 976	4. 032	65. 444	1. 00 16. 83
	ATOM	1537	C	THR	206	32. 970	7. 258	66. 220	1. 00 24. 75
	ATOM	1538	0	THR	206	34. 025	7. 326	66. 858	1. 00 25. 65
5	ATOM	1539	N	VAL	207	32. 632	8. 136	65. 285	1. 00 22. 49
	ATOM	1540	CA	VAL	207	33. 487	9. 257	64. 917	1. 00 23. 51
	ATOM	1541	CB	VAL	207	32. 775	10. 133	63. 855	1. 00 25. 35
	ATOM	1542	CG	VAL	207	33. 617	11. 362	63. 521	1. 00 24. 61
	ATOM	1543	CG2	VAL	207	32. 509	9. 299	62. 609	1. 00 21. 66
10	ATOM	1544	C	VAL	207	33. 897	10. 119	66. 126	1. 00 23. 48
	ATOM	1545	0	VAL	207	35. 061	10. 470	66. 279	1. 00 26. 51
	ATOM	1546	N	ALA	208	32. 948	10. 452	66. 989	1. 00 24. 53
	ATOM	1547	CA	ALA	208	33. 262	11. 251	68. 169	1. 00 26. 32
	ATOM	1548	CB	ALA	208	31. 980	11533	68. 958	1. 00 27. 56
15	ATOM	1549	C	ALA	208	34. 287	10. 530	69. 055	1. 00 28. 84
	ATOM	1550	0	ALA	208	35. 247	11. 138	69. 549	1. 00 27. 69
	ATOM	1551	N	THR	209	34. 084	9. 228	69. 258	1. 00 28. 76
	ATOM	1552	CA	THR	209	35. 006	8. 447	70. 075	1. 00 28. 08
	ATOM	1553	CB	THR	209	34. 474	7. 001	70. 271	1. 00 31. 76
20	ATOM	1554	0G1	THR	209	33. 373	7. 027	71. 181	1. 00 33. 12
	ATOM	1555	CG2	THR	209	35. 550	6. 080	70. 818	1. 00 30. 03
	ATOM	1556	C	THR	209	36. 382	8. 414	69. 418	1. 00 26. 73
	ATOM	1557	0	THR	209	37. 399	8. 611	70. 078	1. 00 28. 00
	ATOM	1558	N	MET	210	36. 421	8. 191	68. 110	1. 00 28. 44
25	ATOM	1559	CA	MET	210	37. 703	8. 143	67. 419	1. 00 28. 08
	ATOM	1560	CB	MET	210	37. 516	7. 851	65. 932	1. 00 26. 94
	ATOM	1561	CG	MET	210	38. 842	7. 766	65. 168	1. 00 28. 59
	ATOM	1562	SD	MET	210	38. 643	7. 734	63. 374	1. 00 32. 14
	ATOM	1563	CE	MET	210	38. 216	9. 518	63. 083	1. 00 33. 30

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	ATOM	1564	C	MET	210	38. 467	9. 452	67. 578	1. 00 29. 43
	ATOM	1565	0	MET	210	39. 636	9. 459	67. 972	1. 00 30. 57
	ATOM	1566	N	ILE	211	37. 799	10. 561	67. 281	1. 00 31. 16
	ATOM	1567	CA	ILE	211	38. 433	11. 873	67. 376	1. 00 30. 57
5	ATOM	1568	CB	ILE	211	37. 418	13. 012	67. 019	1. 00 29. 75
	ATOM	1569	CG	2 ILE	211	38. 086	14. 390	67. 177	1. 00 28. 08
	ATOM	1570	CG	I ILE	211	36. 928	12. 837	65. 578	1. 00 22. 83
	ATOM	1571	CD	ILE	211	38. 021	12. 979	64. 553	1. 00 26. 28
	ATOM	1572	C	ILE	211	39. 014	12. 128	68. 762	1. 00 30. 30
10	ATOM	1573	0	ILE	211	40. 185	12. 489	68. 897	1. 00 31. 89
	ATOM	1574	N	SER	212	38. 203	11. 914	69. 792	1. 00 32. 78
	ATOM	1575	CA	SER	212	38. 639	12. 146	71. 164	1. 00 35. 84
	ATOM	1576	CB	SER	212	37. 499	11. 852	72. 140	1. 00 35. 91
	ATOM	1577	0G	SER	212	37. 317	10. 455	72. 307	1. 00 41. 55
15	ATOM	1578	C	SER	212	39. 864	11. 334	71. 566	1. 00 37. 74
	ATOM	1579	0	SER	212	40. 684	11. 803	72. 354	1. 00 41. 44
	ATOM	1580	N	CYS	213	39. 990	10. 121	71. 040	1. 00 38. 07
	ATOM	1581	CA	CYS	213	41. 132	9. 273	71. 374	1. 00 39. 83
	ATOM	1582	CB	CYS	213	40. 802	7. 799	71. 108	1. 00 38. 31
20	ATOM	1583	SG	CYS	213	39. 513	7. 129	72. 185	1. 00 38. 48
	ATOM	1584	C	CYS	213	42. 372	9. 666	70. 582	1. 00 41. 86
	ATOM	1585	0	CYS	213	43. 503	9. 426	71. 012	1. 00 38. 47
	ATOM	1586	N	TYR	214	42. 149	10. 261	69. 413	1. 00 45. 32
	ATOM	1587	CA	TYR	214	43. 243	10. 701	68. 554	1. 00 45. 02
25	ATOM	1588	CB	TYR	214	42. 705	11. 506	67. 370	1. 00 45. 88
	ATOM	1589	CG	TYR	214	43. 798	12. 171	66. 573	1. 00 45. 72
	ATOM	1590	CD1	TYR	214	44. 509	11. 465	65. 608	1. 00 46. 39
	ATOM	1591	CE1	TYR	214	45. 556	12. 061	64. 913	1. 00 47. 16
	ATOM	1592	CD2	TYR	214	44. 160	13. 498	66. 823	1. 00 44. 53

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	ATOM	1593	CE2	TYR	214	45. 203	14. 099	66. 134	1. 00 45. 20
	ATOM	1594	CZ	TYR	214	45. 896	13. 375	65. 183	1. 00 46. 22
	ATOM	1595	ОН	TYR	214	46. 942	13. 955	64. 510	1. 00 50. 31
	ATOM	1596	С	TYR	214	44. 226	11. 573	69. 322	1. 00 44. 69
5	ATOM	1597	0	TYR	214	45. 420	11. 296	69. 363	1. 00 44. 40
	ATOM	1598	N	TYR	215	43. 713	12. 635	69. 924	1. 00 45. 92
	ATOM	1599	CA	TYR	215	44. 556	13. 552	70. 667	1. 00 48. 38
	ATOM	1600	CB	TYR	215	43. 713	14. 716	71. 175	1. 00 51. 93
	ATOM	1601	CG	TYR	215	43. 192	15. 545	70. 021	1. 00 57. 70
10	ATOM	1602	CD1	TYR	215	41. 918	15. 330	69. 484	1. 00 58. 41
	ATOM	1603	CE1	TYR	215	41. 478	16. 047	68. 363	1. 00 61. 27
	ATOM	1604	CD2	TYR	215	44. 011	16. 498	69. 413	1. 00 59. 13
	ATOM	1605	CE2	TYR	215	43. 586	17. 214	68. 300	1. 00 61. 22
	ATOM	1606	CZ	TYR	215	42. 325	16. 991	67. 780	1. 00 62. 20
15	ATOM	1607	ОН	TYR	215	41. 928	17. 728	66. 688	1. 00 61. 67
	ATOM	1608	C	TYR	215	45. 304	12. 871	71. 792	1. 00 48. 87
	ATOM	1609	0	TYR	215	46. 282	13. 407	72. 318	1. 00 49. 38
•	ATOM	1610	N	GLU	216	44. 852	11. 672	72. 142	1. 00 47. 69
	ATOM	1611	CA	GLU	216	45. 496	10. 889	73. 181	1. 00 47. 03
20	ATOM	1612	CB	GLU	216	44. 474	9. 979	73. 863	1. 00 49. 83
	ATOM	1613	CG	GLU	216	44. 837	9. 550	75. 270	1. 00 55. 37
	ATOM	1614	CD	GLU	216	44. 998	10. 735	76. 208	1. 00 59. 31
	ATOM	1615	0E1	GLU	216	44. 285	11. 747	76. 012	1. 00 59. 95
	ATOM	1616	0E2	GLU	216	45. 824	10. 649	77. 146	1. 00 60. 13
25	ATOM	1617	C	GLU	216	46. 552	10. 044	72. 477	1. 00 45. 45
	ATOM	1618	0	GLU	216	47. 673	9. 905	72. 958	1. 00 45. 05
	ATOM	1619	N	ASP	217	46. 183	9. 495	71. 321	1. 00 43. 73
	ATOM	1620	CA	ASP	217	47. 074	8. 643	70. 530	1. 00 41. 33
	ATOM	1621	CB	ASP	217	46. 776	7. 171	70. 845	1. 00 40. 13

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	ATOM	1622	CG	ASP	217	47. 780	6. 208	70. 226	1. 00 39. 76
	ATOM	1623	OD	1 ASP	217	48. 461	6. 571	69. 249	1. 00 40. 95
	ATOM	1624	OD	2 ASP	217	47. 876	5. 062	70. 712	1. 00 42. 61
	ATOM	1625	C	ASP	217	46. 852	8. 921	69. 033	1. 00 40. 53
5	ATOM	1626	0	ASP	217	45. 862	8. 474	68. 443	1. 00 37. 20
	ATOM	1627	N	HIS	218	47. 779	9. 657	68. 427	1. 00 41. 94
	ATOM	1628	CA	HIS	218	47. 689	10. 008	67. 007	1. 00 44. 23
	ATOM	1629	CB	HIS	218	48. 912	10. 828	66. 603	1. 00 47. 00
	ATOM	1630	CG	HIS	218	48. 860	12. 244	67. 079	1. 00 51. 95
10	ATOM	1631	CD2	2 HIS	218	49. 230	13. 402	66. 483	1. 00 54. 47
	ATOM	1632	ND	HIS	218	48. 371	12. 592	68. 320	1. 00 54. 33
	ATOM	1633	CE	HIS	218	48. 439	13. 903	68. 467	1. 00 55. 83
	ATOM	1634	NE2	HIS	218	48. 957	14. 419	67. 367	1. 00 55. 95
	ATOM	1635	C	HIS	218	47. 528	8. 810	66. 074	1. 00 42. 66
15	ATOM	1636	0	HIS	218	47. 157	8. 963	64. 909	1. 00 42. 00
	ATOM	1637	N	GLN	219	47. 793	7. 620	66. 597	1. 00 41. 40
	ATOM	1638	CA	GLN	219	47. 667	6. 394	65. 820	1. 00 41. 15
	ATOM	1639	CB	GLN	219	48. 592	5. 321	66. 397	1. 00 45. 16
	ATOM	1640	CG	GLN	219	50. 070	5. 611	66. 214	1. 00 49. 72
20	ATOM	1641	CD	GLN	219	50. 566	5. 230	64. 832	1. 00 55. 92
	ATOM	1642	0E1	GLN	219	49. 997	5. 646	63. 813	1. 00 57. 28
	ATOM	1643	NE2	GLN	219	51. 636	4. 429	64. 787	1. 00 57. 32
	ATOM	1644	C	GLN	219	46. 228	5. 869	65. 792	1. 00 37. 41
	ATOM	1645	0	GLN	219	45. 927	4. 904	65. 091	1. 00 37. 06
25	ATOM	1646	N	CYS	220	45. 342	6. 488	66. 562	1. 00 34. 18
	ATOM	1647	CA	CYS	220	43. 955	6. 038	66. 578	1. 00 32. 52
	ATOM	1648	CB	CYS	220 .	43. 199	6. 597	67. 783	1. 00 28. 93
	ATOM	1649	SG	CYS	220	41. 420	6. 288	67. 739	1. 00 31. 90
,	ATOM	1650	C	CYS	220	43. 272	6. 474	65. 303	1. 00 32. 01

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	ATOM	1651	0	CYS	220	43. 010	7. 664	65. 096	1. 00 32. 91
	ATOM	1652	N	GLU	221	42. 993	5. 505	64. 442	1. 00 29. 12
	ATOM	1653	CA	GLU	221	42. 343	5. 785	63. 176	1. 00 28. 98
	ATOM	1654	CB	GLU	221	43. 273	5. 437	62. 009	1. 00 30. 00
5	ATOM	1655	CG	GLU	221	44. 481	6. 366	61. 853	1. 00 35. 29
	ATOM	1656	CD	GLU	221	45. 190	6. 166	60. 515	1. 00 36. 83
	ATOM	1657	0E 1	GLU	221	44. 490	6. 007	59. 498	1. 00 38. 09
	ATOM	1658	0E2	C GLU	221	46. 436	6. 176	60. 465	1. 00 40. 80
	ATOM	1659	C	GLU	221	41. 057	4. 991	63. 059	1. 00 25. 46
10	ATOM	1660	0	GLU	221	40. 513	4. 835	61. 970	1. 00 22. 65
	ATOM	1661	N	VAL	222	40. 569	4. 491	64. 185	1. 00 25. 43
	ATOM	1662	CA	VAL	222	39. 337	3. 703	64. 179	1. 00 25. 45
	ATOM	1663	CB	VAL	222	39. 625	2. 172	64. 189	1. 00 24. 36
	ATOM	1664	CG1	VAL	222	38. 318	1. 391	64. 122	1. 00 21. 56
15	ATOM	1665	CG2	VAL	222	40. 533	1. 795	63. 029	1. 00 21. 70
	ATOM	1666	C	VAL	222	38. 527	4. 016	65. 414	1. 00 25. 44
	ATOM	1667	0	VAL	222	39. 076	4. 192	66. 492	1. 00 25. 99
	ATOM	1668	N	GLY	223	37. 217	4. 090	65. 240	1. 00 25. 97
	ATOM	1669	CA	GLY	223	36. 328	4. 347	66. 349	1. 00 25. 83
20	ATOM	1670	С	GLY	223	35. 337	3. 201	66. 340	1. 00 25. 37
	ATOM	1671	0	GLY	223	34. 852	2. 812	65. 273	1. 00 25. 38
	ATOM	1672	N	MET	224	35. 044	2. 647	67. 511	1. 00 24. 88
	ATOM	1673	CA	MET	224	34. 114	1. 527	67. 587	1. 00 25. 47
	ATOM	1674	CB	MET	224	34. 881	0. 187	67. 638	1. 00 22. 66
25	ATOM	1675	CG	MET	224	33. 956	-1. 041	67. 634	1. 00 25. 14
	ATOM	1676	SD	MET	224	34. 806	-2. 680	67. 748	1. 00 22. 18
	ATOM	1677	CE	MET	224	35. 380	-2. 594	69. 396	1. 00 16. 01
	ATOM	1678	C	MET	224	33. 177	1. 618	68. 780	1. 00 22. 20
	ATOM	1679	0	MET	224	33. 577	1. 978	69. 881	1. 00 22. 65

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	ATOM	1680	N	ILE	225	31. 915	1. 295	68. 543	1. 00 21. 12
	ATOM	1681	CA	ILE	225	30. 936	1. 314	69. 604	1. 00 21. 34
	ATOM	1682	CB	ILE	225	29. 757	2. 295	69. 293	1. 00 25. 85
	ATOM	1683	CG2	ILE	225	28. 739	2. 268	70. 446	1. 00 25. 47
5	ATOM	1684	CG1	ILE	225	30. 273	3. 734	69. 107	1. 00 25. 08
	ATOM	1685	CD1	ILE	225	30. 838	4. 355	70. 382	1. 00 22. 09
	ATOM	1686	C	ILE	225	30. 321	-0. 080	69. 789	1. 00 22. 30
	ATOM	1687	0	ILE	225	29. 885	-0. 712	68. 826	1. 00 24. 03
	ATOM	1688	N	VAL	226	30. 313	-0. 563	71. 025	1. 00 22. 67
10	ATOM	1689	CA	VAL	226	29. 645	-1. 817	71. 341	1. 00 21. 60
	ATOM	1690	CB	VAL	226	30. 618	-2. 993	71. 634	1. 00 21. 77
	ATOM	1691	CG1	VAL	226	29. 821	-4. 291	71. 718	1. 00 21. 54
	ATOM	1692	CG2	VAL	226	31.663	-3. 113	70. 541	1. 00 17. 23
	ATOM	1693	C	VAL	226	28. 838	-1. 493	72. 604	1. 00 21. 49
15	ATOM	1694	0	VAL	226	29. 316	-1. 633	73. 723	1. 00 18. 90
	ATOM	1695	N	GLY	227	27. 615	-1. 016	72. 402	1. 00 25. 39
	ATOM	1696	CA	GLY	227	26. 744	-0. 675	73. 518	1. 00 26. 76
	ATOM	1697	C	GLY	227	25. 353	-1. 140	73. 150	1. 00 28. 03
	ATOM	1698	0	GLY	227	25. 155	-2. 315	72. 846	1. 00 29. 80
20	ATOM	1699	N	THR	228	24. 384	-0. 235	73. 161	1. 00 27. 62
	ATOM	1700	CA	THR	228	23. 031	-0. 607	72. 788	1. 00 27. 59
	ATOM	1701	CB	THR	228	22. 083	0. 601	72. 911	1. 00 29. 15
	ATOM	1702	0G1	THR	228	21. 937	0. 932	74. 294	1. 00 32. 52
	ATOM	1703	CG2	THR	228	20. 719	0. 291	72. 339	1. 00 28. 08
25	ATOM	1704	C	THR	228	23. 094	-1. 080	71. 345	1. 00 26. 98
	ATOM	1705	0	THR	228	22. 460	-2. 065	70. 960	1. 00 27. 95
	ATOM	1706	N	GLY	229	23. 890	-0. 374	70. 554	1. 00 26. 02
	ATOM	1707	CA	GLY	229	24. 050	-0. 718	69. 154	1. 00 25. 33
	ATOM	1708	C	GLY	229	25. 503	-1. 055	68. 911	1. 00 24. 09

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	ATOM	1709	0	GLY	229	26. 312	-1. 004	69. 838	1. 00 23. 25
	ATOM	1710	N	CYS	230	25. 850	-1. 395	67. 677	1. 00 24. 12
	ATOM	1711	CA	CYS	230	27. 235	-1. 750	67. 376	1. 00 23. 83
	ATOM	1712	CB	CYS	230	27. 395	-3. 280	67. 425	1. 00 20. 39
5	ATOM	1713	SG	CYS	230	29. 076	-3. 879	67. 182	1. 00 25. 34
	ATOM	1714	C	CYS	230	27. 627	-1. 204	66. 010	1. 00 20. 45
	ATOM	1715	0	CYS	230	26. 919	-1. 406	65. 035	1. 00 20. 28
	ATOM	1716	N	ASN	231	28. 763	-0. 526	65. 935	1. 00 23. 86
	ATOM	1717	CA	ASN	231	29. 196	0. 076	64. 669	1. 00 24. 35
10	ATOM	1718	CB	ASN	231	28. 267	1. 261	64. 355	1. 00 25. 51
	ATOM	1719	CG	ASN	231	28. 598	1. 962	63. 042	1. 00 27. 76
	ATOM	1720	0D 1	ASN	231	28. 930	1. 331	62. 039	1. 00 24. 60
	ATOM	1721	ND2	ASN	231	28. 472	3. 288	63. 043	1. 00 30. 91
	ATOM	1722	C	ASN	231	30. 640	0. 553	64. 784	1. 00 23. 81
15	ATOM	1723	0	ASN	231	31. 184	0. 624	65. 885	1. 00 23. 94
,	ATOM	1724	N	ALA	232	31. 249	0. 885	63. 651	1. 00 22. 70
	ATOM	1725	CA	ALA	232	32. 626	1. 359	63. 636	1. 00 25. 15
	ATOM	1726	CB	ALA	232	33. 580	0. 169	63. 463	1. 00 24. 36
	ATOM	1727	C	ALA	232	32. 867	2. 372	62. 511	1. 00 26. 31
20	ATOM	1728	0	ALA	232	32. 127	2. 416	61. 530	1. 00 28. 47
	ATOM	1729	N	CYS	233	33. 911	3. 176	62. 664	1. 00 24. 88
	ATOM	1730	CA	CYS	233	34. 291	4. 160	61. 653	1. 00 26. 51
	ATOM	1731	CB	CYS	233	33. 899	5. 583	62. 076	1. 00 24. 89
	ATOM	1732	SG	CYS	233	34. 875	6. 224	63. 436	1. 00 25. 76
25	ATOM	1733	C	CYS	233	35. 805	4. 055	61. 555	1. 00 25. 08
	ATOM	1734	0	CYS	233	36. 450	3. 564	62. 480	1. 00 25. 19
	ATOM	1735	N	TYR	234	36. 373	4. 505	60. 442	1. 00 25. 32
	ATOM	1736	CA	TYR	234	37. 820	4. 427	60. 245	1. 00 23. 93
	ATOM	1737	CB	TYR	234	38. 200	3. 020	59. 760	1. 00 20. 70

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	ATOM	1738	CG	TYR	234	37. 782	2. 771	58. 328	1. 00 16. 7	78
	ATOM	1739	CD1	TYR	234	38. 712	2. 786	57. 302	1. 00 18. 7	'5
	ATOM	1740	CE1	TYR	234	38. 326	2. 668	55. 975	1. 00 18. 8	39
	ATOM	1741	CD2	TYR	234	36. 443	2. 622	57. 990	1. 00 19. 6	0
5	ATOM	1742	CE2	TYR	234	36. 043	2. 506	56. 666	1. 00 18. 4	10
	ATOM	1743	CZ	TYR	234	36. 990	2. 535	55. 665	1. 00 21. 5	5
	ATOM	1744	ОН	TYR	. 234	36. 603	2. 479	54. 346	1. 00 23. 2	:5
	ATOM	1745	C	TYR	234	38. 254	5. 452	59. 194	1. 00 26. 4	1
	ATOM	1746	0	TYR	234	37. 436	5. 929	58. 404	1. 00 27. 1	4
10	ATOM	1747	N	MET	235	39. 543	5. 769	59. 179	1. 00 27. 1	0
	ATOM	1748	CA	MET	235	40. 094	6. 722	58. 224	1. 00 28. 7	4
	ATOM	1749	CB	MET	235	41. 383	7. 331	58. 789	1. 00 29. 3	8
	ATOM	1750	CG	MET	235	41. 169	8. 180	60. 035	1. 00 31. 4	3
	ATOM	1751	SD	MET	235	39. 947	9. 503	59. 750	1. 00 32. 3	0
15	ATOM	1752	CE	MET	235	40. 866	10. 535	58. 591	1. 00 34. 1	1
	ATOM	1753	C	MET	235	40. 374	6.066	56. 869	1. 00 29. 4	2
	ATOM	1754	0	MET	235	41. 170	5. 134	56. 767	1. 00 30. 4	9
	ATOM	1755	N	GLU	236	39. 714	6. 565	55. 829	1. 00 31. 0	8
	ATOM	1756	CA	GLU	236	39. 867	6. 040	54. 476	1. 00 31. 0	4
20	ATOM	1757	CB	GLU	236	38. 491	5. 743	53. 879	1. 00 31. 5	7
	ATOM	1758	CG	GLU	236	38. 536	5. 161	52. 474	1. 00 32. 1	8
	ATOM	1759	CD	GLU	236	39. 330	3. 875	52. 427	1. 00 32. 5	2
	ATOM	1760	0E1	GLU	236	40. 565	3. 952	52. 273	1. 00 34. 3	4
	ATOM	1761	0E2	GLU	236	38. 723	2. 789	52. 571	1. 00 30. 7	9
25	ATOM	1762	C	GLU	236	40. 598	7. 030	53. 574	1. 00 33. 4	3
	ATOM	1763	0	GLU	236	40. 583	8. 238	53. 818	1. 00 29. 9	3
	ATOM	1764	N	GLU	237	41. 240	6. 506	52. 532	1. 00 35. 8	5
	ATOM	1765	CA	GLU	237	41. 969	7. 333	51. 575	1. 00 37. 83	3
	ATOM	1766	CB	GLU	237	42. 934	6. 462	50. 764	1. 00 40. 10	6

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	ATOM	1767	CG	GLU	237	43. 684	5. 426	51. 602	1. 00	43. 86
	ATOM	1768	CD	GLU	237	44. 466	6. 049	52. 743	1. 00	47. 85
	ATOM	1769	0E1	GLU	237	44. 806	5. 322	53. 704	1. 00	51. 02
	ATOM	1770	0E2	GLU	237	44. 747	7. 264	52. 681	1. 00	48. 78
5	ATOM	1771	C	GLU	237	40. 920	7. 969	50. 657	1. 00	37. 87
	ATOM	1772	0	GLU	237	40. 058	7. 268	50. 122	1. 00	38. 29
	ATOM	1773	N	MET	238	40. 987	9. 287	50. 477	1. 00	37. 42
	ATOM	1774	CA	MET	238	40. 009	9. 987	49. 644	1. 00	37. 50
	ATOM	1775	CB	MET	238	40. 375	11. 467	49. 501	1. 00	38. 62
10	ATOM	1776	CG	MET	238	39. 772	12. 355	50. 587	1. 00	40. 32
	ATOM	1777	SD	MET	238	37. 956	12. 144	50. 764	1. 00	42. 83
	ATOM	1778	CE	MET	238	37. 308	13. 116	49. 410	1. 00	44. 06
	ATOM	1779	C	MET	238	39. 796	9. 374	48. 270	1. 00	36. 21
	ATOM	1780	0	MET	238	38. 685	9. 413	47. 740	1. 00	33. 93
15	ATOM	1781	N	GLN	239	40. 848	8. 803	47. 690	1. 00	35. 50
	ATOM	1782	CA	GLN	239	40. 714	8. 184	46. 378	1. 00	36. 82
	ATOM	1783	CB	GLN	239	42. 078	7. 732	45. 846	1. 00	39. 35
	ATOM	1784	CG	GLN	239	42. 839	6. 804	46. 774	1. 00	44. 12
	ATOM	1785	CD	GLN	239	43. 900	7. 534	47. 584	1. 00	49. 18
20	ATOM	1786	0E1	GLN	239	43. 635	8. 580	48. 192	1. 00	49. 88
	ATOM	1787	NE2	GLN	239	45. 111	6. 981	47. 600	1. 00	49. 95
	ATOM	1788	C	GLN	239	39. 762	6. 986	46. 395	1. 00	35. 72
	ATOM	1789	0	GLN	239	39. 276	6. 568	45. 348	1. 00	37. 20
	ATOM	1790	N	ASN	240	39. 503	6. 419	47. 570	1. 00	34. 56
25	ATOM	1791	CA	ASN	240	38. 604	5. 272	47. 648	1. 00	33. 20
	ATOM	1792	CB	ASN	240	39. 118	4. 239	48. 658	1. 00	33. 68
	ATOM	1793	CG	ASN	240	40. 548	3. 802	48. 369	1. 00	34. 24
	ATOM	1794	0D1	ASN	240	40. 963	3. 710	47. 210	1. 00	33. 87
	ATOM	1795	ND2	ASN	240	41. 306	3. 523	49. 424	1. 00	34. 32

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	ATOM	1796	C	ASN	240	37. 190	5. 690	48. 011	1. 00	33. 25
	ATOM	1797	0	ASN	240	36. 259	4. 886	47. 936	1. 00	33. 86
	ATOM	1798	N	VAL	241	37. 024	6. 946	48. 414	1. 00	32. 52
	ATOM	1799	CA	VAL	241	35. 702	7. 441	48. 753	1. 00	31. 62
5	ATOM	1800	CB	VAL .	241	35. 755	8. 559	49. 811	1. 00	29. 14
	ATOM	1801	CG1	VAL	241	34. 339	8. 948	50. 204	1. 00	31. 00
	ATOM	1802	CG2	VAL	241	36. 530	8. 107	51. 021	1. 00	26. 87
	ATOM	1803	C	VAL	241	35. 102	8. 010	47. 474	1. 00	33. 73
	ATOM	1804	0	VAL	241	35. 048	9. 224	47. 286	1. 00	35. 18
10	ATOM	1805	N	GLU	242	34. 643	7. 132	46. 595	1. 00	33. 33
	ATOM	1806	CA	GLU	242	34. 075	7. 572	45. 324	1. 00	33. 69
	ATOM	1807	CB	GLU	242	33. 788	6. 364	44. 431	1. 00	31. 05
	ATOM	1808	CG	GLU	242	34. 983	5. 457	44. 222	1. 00	33. 00
	ATOM	1809	CD	GLU	242	34. 767	4. 451	43. 115	1. 00	33. 45
15	ATOM	1810	0E1	GLU	242	33. 595	4. 162	42. 776	1. 00	33. 74
	ATOM	1811	0E2	GLU	242	35. 778	3. 940	42. 592	1. 00	35. 96
	ATOM	1812	C	GLU	242	32. 812	8. 437	45. 427	1. 00	34. 45
	ATOM	1813	0.	GLU	242	32. 406	9. 061	44. 442	1. 00	32. 92
	ATOM	1814	N	LEU	243	32. 192	8. 471	46. 602	1. 00	33. 82
20	ATOM	1815	CA	LEU	243	30. 982	9. 262	46. 799	1. 00	36. 13
	ATOM	1816	CB	LEU	243	30. 080	8. 598	47. 844	1. 00	33. 99
	ATOM	1817	CG	LEU	243	29. 168	7. 490	47. 297	1. 00	37. 04
	ATOM	1818	CD1	LEU	243	27. 999	8. 096	46. 545	1. 00	36. 01
	ATOM	1819	CD2	LEU	243	29. 969	6. 560	46. 384	1. 00	36. 49
25	ATOM	1820	C	LEU	243	31. 290	10. 700	47. 199	1. 00	35. 69
	ATOM	1821	.0	LEU	243	30. 406	11. 458	47. 585	1. 00	37. 51
	ATOM	1822	N	VAL	244	32. 560	11. 062	47. 117	1. 00	37. 53
	ATOM	1823	CA	VAL	244	32. 992	12. 411	47. 426	1. 00	37. 50
	ATOM	1824	CB	VAL	244	33. 537	12. 547	48. 861	1. 00	36. 75

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	ATOM	1825	CG1	VAL	244	33. 967	13. 990	49. 109	1. 00	36. 55
	ATOM	1826	CG2	VAL	244	32. 465	12. 160	49. 870	1. 00	37. 02
	ATOM	1827	C	VAL	244	34. 099	12. 727	46. 446	1. 00	39. 75
	ATOM	1828	0	VAL	244	35. 090	12. 003	46. 361	1. 00	39. 55
5	ATOM	1829	N	GLU	245	33. 909	13. 802	45. 688	1. 00	42. 16
	ATOM	1830	CA	GLU	245	34. 880	14. 232	44. 695	1. 00	42. 30
	ATOM	1831	CB	GLU	245	34. 372	15. 487	43. 989	1. 00	45. 34
	ATOM	1832	CG	GLU	245	34. 886	15. 636	42. 576	1. 00	48. 54
	ATOM	1833	CD	GLU	245	34. 377	16. 893	41. 901	1. 00	50. 12
10	ATOM	1834	0E1	GLU	245	33. 192	17. 249	42. 107	1. 00	49. 37
	ATOM	1835	OE2	GLU	245	35. 164	17. 511	41. 152	1. 00	52. 40
	ATOM	1836	C	GLU	245	36. 203	14. 532	45. 378	1. 00	41.00
	ATOM	1837	0	GLU	245	36. 230	15. 132	46. 446	1. 00	42. 20
	ATOM	1838	N	GLY	246	37. 297	14. 107	44. 761	1. 00	41. 28
15	ATOM	1839	CA	GLY	246	38. 606	14. 349	45. 336	1. 00	42. 88
	ATOM	1840	C	GLY	246	39. 362	13. 066	45. 618	1. 00	45. 38
	ATOM	1841	0	GLY	246	38. 774	12. 056	45. 997	1. 00	45. 50
	ATOM	1842	N	ASP	247	40. 675	13. 105	45. 443	1. 00	47. 31
	ATOM	1843	CA	ASP	247	41. 509	11. 940	45. 687	1. 00	49. 13
20	ATOM	1844	CB	ASP	247	42. 139	11. 454	44. 384	1. 00	51.65
	ATOM	1845	CG	ASP	247	41. 131	10. 836	43. 449	1. 00	56. 09
	ATOM	1846	OD1	ASP	247	41. 534	10. 410	42. 345	1. 00	58. 83
	ATOM	1847	OD2	ASP	247	39. 936	10. 770	43. 819	1. 00	59. 44
	ATOM	1848	C	ASP	247	42. 611	12. 274	46. 667	1. 00	49. 51
25	ATOM	1849	0	ASP	247	43. 406	11. 415	47. 039	1. 00	49. 57
	ATOM	1850	N	GLU	248	42. 661	13. 531	47. 086	1. 00	50. 49
	ATOM	1851	CA	GLU	248	43. 696	13. 957	48. 011	1. 00	50. 97
	ATOM	1852	CB	GLU	248	44. 198	15. 351	47. 634	1. 00	54. 71
	ATOM	1853	CG	GLU	248	45. 670	15. 391	47. 259	1. 00	62. 15

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	ATOM	1854	CD	GLU	248	46. 067	14. 259	46. 317	1. 00 66. 63
	ATOM	1855	0E1	GLU	248	46. 196	13. 105	46. 788	1. 00 68. 58
	ATOM	1856	0E2	GLU	248	46. 241	14. 520	45. 105	1. 00 68. 21
	ATOM	1857	C	GLU	248	43. 222	13. 955	49. 446	1. 00 47. 90
5	ATOM	1858	0	GLU	248	42. 063	14. 250	49. 726	1. 00 46. 55
	ATOM	1859	N	GLY	249	44. 133	13. 614	50. 351	1. 00 45. 49
	ATOM	1860	CA	GLY	249	43. 799	13. 590	51. 759	1. 00 44. 30
	ATOM	1861	C	GLY	249	43. 138	12. 301	52. 205	1. 00 42. 85
	ATOM	1862	0	GLY	249	43. 257	11. 259	51. 552	1. 00 42. 97
10	ATOM	1863	N	ARG	250	42. 444	12. 380	53. 335	1. 00 41. 43
	ATOM	1864	CA	ARG	250	41. 747	11. 232	53. 897	1. 00 39. 63
	ATOM	1865	CB	ARG	250	42. 625	10. 532	54. 931	1. 00 40. 69
	ATOM	1866	CG	ARG	250	44. 092	10. 454	54. 559	1. 00 43. 91
	ATOM	1867	CD	ARG	250	44. 903	9. 902	55. 714	1. 00 45. 22
15	ATOM	1868	NE	ARG	250	44. 630	8. 487	55. 940	1. 00 45. 43
	ATOM	1869	CZ	ARG	250	45. 040	7. 813	57. 007	1. 00 44. 67
	ATOM	1870	NH1	ARG	250	45. 738	8. 426	57. 954	1. 00 46. 95
	ATOM	1871	NH2	ARG	250	44. 761	6. 524	57. 121	1. 00 46. 99
	ATOM	1872	C	ARG	250	40. 486	11. 726	54. 580	1. 00 37. 70
20	ATOM	1873	0	ARG	250	40. 430	12. 865	55. 042	1. 00 37. 51
	ATOM	1874	N	MET	251	39. 473	10. 867	54. 630	1. 00 35. 10
	ATOM	1875	CA	MET	251	38. 216	11. 197	55. 277	1. 00 32. 34
	ATOM	1876	CB	MET	251	37. 137	11. 517	54. 242	1. 00 33. 00
	ATOM	1877	CG	MET	251	35. 803	11. 907	54. 868	1. 00 31. 56
25	ATOM	1878	SD	MET	251	34. 474	12. 160	53. 677	1. 00 37. 84
	ATOM	1879	CE	MET	251	35. 067	13. 715	52. 885	1. 00 32. 92
	ATOM	1880	C	MET	251	37. 764	10. 007	56. 121	1. 00 32. 47
	ATOM	1881	0	MET	251	38. 024	8. 852	55. 777	1. 00 31. 05
	ATOM	1882	N	CYS	252	37. 088	10. 292	57. 229	1. 00 30. 16

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	ATOM	1883	CA	CYS	252	36. 595	9. 236	58. 092	1. 00 30. 32
	ATOM	1884	CB	CYS	252	36. 364	9. 762	59. 517	1. 00 30. 54
	ATOM	1885	SG	CYS	252	35. 601	8. 557	60. 676	1. 00 28. 61
	ATOM	1886	C	CYS	252	35. 292	8. 717	57. 511	1. 00 29. 86
5	ATOM	1887	0	CYS	252	34. 422	9. 495	57. 114	1. 00 29. 84
	ATOM	1888	N	VAL	253	35. 170	7. 397	57. 438	1. 00 28. 79
	ATOM	1889	CA	VAL	253	33. 960	6. 776	56. 921	1. 00 27. 69
	ATOM	1890	CB	VAL	253	34. 291	5. 761	55. 816	1. 00 28. 07
	ATOM	1891	CG1	VAL	253	33. 033	5. 005	55. 405	1. 00 26. 98
10	ATOM	1892	CG2	VAL	253	34. 898	6. 484	54. 624	1. 00 24. 14
	ATOM	1893	C	VAL	253	33. 200	6. 069	58. 038	1. 00 28. 79
	ATOM	1894	0	VAL	253	33. 801	5. 448	58. 922	1. 00 31. 23
•	ATOM	1895	N	ASN	254	31. 879	6. 188	58. 000	1. 00 28. 38
	ATOM	1896	CA	ASN	254	31. 003	5. 557	58. 976	1. 00 27. 73
15	ATOM	1897	CB	ASN	254	29. 834	6. 473	59. 328	1. 00 27. 41
	ATOM	1898	CG	ASN	254	28. 803	5. 779	60. 181	1. 00 31.67
	ATOM	1899	OD1	ASN	254	29. 048	4. 675	60. 677	1. 00 32. 14
	ATOM	1900	ND2	ASN	254	27. 643	6. 415	60. 367	1. 00 29. 17
	ATOM	1901	C	ASN	254	30. 480	4. 295	58. 299	1. 00 27. 41
20	ATOM	1902	0	ASN	254	29. 575	4. 372	57. 467	1. 00 25. 53
	ATOM	1903	N	THR	255	31. 049	3. 142	58. 654	1. 00 24. 66
	ATOM	1904	CA	THR	255	30. 662	1. 883	58. 016	1. 00 24. 86
	ATOM	1905	CB	THR	255	31. 501	0. 665	58. 527	1. 00 23. 42
	ATOM	1906	0G1	THR	255	31. 071	0. 310	59. 849	1. 00 23. 50
25	ATOM	1907	CG2	THR	255	32. 973	0. 982	58. 558	1. 00 23. 88
	ATOM	1908	C	THR	255	29. 207	1. 488	58. 195	1. 00 23. 00
	ATOM	1909	0	THR	255	28. 589	0. 984	57. 259	1. 00 24. 38
	ATOM	1910	N	GLU	256	28. 673	1. 710	59. 394	1. 00 23. 70
	ATOM	1911	CA	GLU	256	27. 306	1. 305	59. 721	1. 00 26. 37

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	ATOM	1912	CB	GLU	256	26. 271	2.017	58. 838	1. 00 26. 22
	ATOM	1913	CG		256				1. 00 29. 32
	ATOM	1914	CD	GLU	256	25. 284			1. 00 31. 10
	ATOM	1915	0E 1	GLU	256				1. 00 31. 47
5	ATOM	1916	0E2	2 GLU	256		4. 682		
	ATOM	1917	C	GLU	256	27. 269		59. 458	
	ATOM	1918	0	GLU	256	26. 369	-0. 713		1. 00 26. 71
	ATOM	1919	N	TRP	257		-0. 912		
	ATOM	1920	CA	TRP	257	28. 335			
10	ATOM	1921	CB	TRP	257	29. 714	-2. 928	60. 180	1. 00 21. 05
	ATOM	1922	CG	TRP	257	30. 100	-2. 891	61. 653	1. 00 17. 51
	ATOM	1923	CD2	TRP	257	31. 429	-3. 026	62. 182	1. 00 16. 19
	ATOM	1924	CE2	TRP	257	31. 320	-3. 077	63. 588	1. 00 14. 42
	ATOM	1925	CE3	TRP	257	32. 705	-3. 112	61. 597	1. 00 16. 23
15	ATOM	1926	CD1	TRP	257	29. 264	-2. 862	62. 733	1. 00 18. 14
	ATOM	1927	NE 1	TRP	257	29. 990	-2. 977	63. 902	1. 00 19. 95
	ATOM	1928	CZ2	TRP	257	32. 435	-3. 214	64. 421	1. 00 17. 46
	ATOM	1929	CZ3	TRP	257	33. 815	-3. 246	62. 424	1. 00 13. 91
	ATOM	1930	CH2	TRP	257	33. 672	-3. 294	63. 822	1. 00 14. 28
20	ATOM	1931	C	TRP	257	27. 218	-3. 091	60. 500	1. 00 24. 58
	ATOM	1932	0	TRP	257	27. 067	-4. 305	60. 352	1. 00 24. 81
	ATOM	1933	N	GLY	258	26. 427	-2. 354	61. 273	1. 00 23. 21
	ATOM	1934	CA	GLY	258	25. 328	-2. 981	61. 982	1. 00 23. 11
	ATOM	1935	C	GLY	258	24. 385	-3. 640	60. 991	1. 00 25. 72
25	ATOM	1936	0	GLY	258	23. 758	-4. 660	61. 285	1. 00 28. 37
	ATOM	1937	N	ALA	259	24. 288	-3.067	59. 796	1. 00 24. 64
	ATOM	1938	CA	ALA	259	23. 406	-3. 630	58. 789	1. 00 25. 53
	ATOM	1939	CB	ALA	259	22. 866	-2. 519	57. 874	1. 00 25. 11
	ATOM	1940	C	ALA	259	24. 084	-4. 724	57. 961	1. 00 25. 44

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	ATOM	1941	0	ALA	259	23. 515	-5. 205	56. 985	1. 00 24. 68
	ATOM	1942	N	PHE	260	25. 306	-5. 101	58. 329	1. 00 26. 96
	ATOM	1943	CA	PHE	260	25. 995	-6. 175	57. 614	1. 00 28. 11
	ATOM	1944	CB	PHE	260	27. 359	-6. 440	58. 254	1. 00 30. 88
5	ATOM	1945	CG	PHE	260	28. 127	-7. 569	57. 625	1. 00 33. 87
	ATOM	1946	CD1	PHE	260	28. 496	-7. 525	56. 286	1. 00 33. 60
	ATOM	1947	CD2	PHE	260	28. 499	-8. 675	58. 380	1. 00 37. 30
	ATOM	1948	CE1	PHE	260	29. 220	-8. 564	55. 716	1. 00 33. 58
	ATOM	1949	CE2	PHE	260	29. 229	-9. 720	57. 808	1. 00 35. 65
10	ATOM	1950	CZ	PHE	260	29. 586	-9. 660	56. 478	1. 00 34. 41
	ATOM	1951	C	PHE	260	25. 080	-7. 388	57. 783	1. 00 28. 87
	ATOM	1952	0	PHE	260	24. 487	-7. 576	58. 849	1. 00 27. 08
	ATOM	1953	N	GLY	261	24. 941	-8. 193	56. 737	1. 00 28. 88
	ATOM	1954	CA	GLY	261	24. 074	-9. 357	56. 826	1. 00 30. 83
15	ATOM	1955	C	GLY	261	22. 664	-9. 092	56. 317	1. 00 32. 15
	ATOM	1956	0	GLY	261	21. 905	-10. 021	56. 043	1. 00 34. 22
	MOTA	1957	N	ASP	262	22. 307	-7. 822	56. 175	1. 00 33. 45
	ATOM	1958	CA	ASP	262	20. 975	-7. 456	55. 701	1. 00 35. 91
	ATOM	1959	CB	ASP	262	20. 761	-5. 948	55. 868	1. 00 35. 78
20	ATOM	1960	CG	ASP	262	20. 674	-5. 541	57. 323	1. 00 35. 93
	ATOM	1961	0D1	ASP	262	20. 903	-6. 415	58. 182	1. 00 37. 70
	ATOM	1962	OD2	ASP	262	20. 382	-4. 364	57. 615	1. 00 35. 14
	ATOM	1963	C	ASP	262	20. 676	-7. 884	54. 262	1. 00 36. 35
	ATOM	1964	0	ASP	262	19. 546	-7. 758	53. 799	1. 00 37. 40
25	ATOM	1965	N	SER	263	21. 685	-8. 380	53. 554	1. 00 37. 07
	ATOM	1966	CA	SER	263	21. 488	-8. 863	52. 189	1. 00 37. 53
	ATOM	1967	CB	SER	263	22. 420	-8. 155	51. 200	1. 00 37. 00
	ATOM	1968	0G	SER	263	22. 028	-6. 815	50. 991	1. 00 38. 85
	ATOM	1969	C	SER	263	21. 770	-10. 359	52. 161	1. 00 37. 06

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	ATOM	1970	0	SER	263	22. 062 -10. 923	51. 107	1. 00 36. 90
	ATOM	1971	N	GLY	264	21. 697 -10. 988	53. 331	1. 00 36. 97
	ATOM	1972	CA	GLY	264	21. 934 -12. 418	53. 428	1. 00 37. 50
	ATOM	1973	C	GLY	264	23. 370 -12. 857	53. 663	1. 00 38. 59
5	ATOM	1974	0	GLY	264	23. 666 -14. 050	53: 573	1. 00 40. 28
	ATOM	1975	N	GLU	265	24. 263 -11. 915	53. 961	1. 00 37. 52
	ATOM	1976	CA	GLU	265	25. 671 -12. 237	54. 199	1. 00 36. 34
	ATOM	1977	CB	GLU	265	26. 488 -10. 965	54. 438	1. 00 35. 82
	ATOM	1978	CG	GLU	265	26. 535 -9. 976	53. 289	1. 00 38. 57
10	ATOM	1979	CD	GLU	265	25. 270 -9. 148	53. 158	1. 00 39. 55
	ATOM	1980	0E 1	GLU	265	24. 600 -8. 901	54. 173	1. 00 38. 51
	ATOM	1981	0E2	GLU	265	24. 953 -8. 722	52. 031	1. 00 43. 82
	ATOM	1982	C	GLU	265	25. 906 -13. 171	55. 391	1. 00 36. 38
	ATOM	1983	0	GLU	265	26. 899 -13. 906	55. 425	1. 00 35. 35
15	ATOM	1984	N	LEU	266	24. 996 -13. 140	56. 362	1. 00 34. 63
	ATOM	1985	CA	LEU	266	25. 130 -13. 955	57. 567	1. 00 35. 02
	ATOM	1986	CB	LEU	266	25. 008 -13. 054	58. 803	1. 00 31. 68
	ATOM	1987	CG	LEU	266	26. 017 -11. 914	58. 973	1. 00 33. 35
	ATOM	1988	CD1	LEU	266	25. 555 -10. 975	60. 077	1. 00 32. 52
20	ATOM	1989	CD2	LEU	266	27. 383 -12. 480	59. 294	1. 00 32. 43
	ATOM	1990	C	LEU	266	24. 108 -15. 092	57. 674	1. 00 35. 37
	ATOM	1991	0	LEU	266	24. 047 -15. 779	58. 696	1. 00 35. 21
	ATOM	1992	N	ASP	267	23. 321 -15. 300	56. 627	1. 00 36. 35
	ATOM	1993	CA	ASP	267	22. 286 -16. 332	56. 643	1. 00 39. 50
25	ATOM	1994	CB	ASP	267	21. 664 -16. 480	55. 248	1. 00 42. 21
	ATOM	1995	CG	ASP	267	20. 666 -15. 369	54. 921	1. 00 45. 43
	ATOM	1996	0D1	ASP	267	20. 205 -15. 320	53. 759	1. 00 48. 41
	ATOM	1997	0D2	ASP	267	20. 332 -14. 554	55. 813	1. 00 45. 57
	ATOM	1998	C	ASP	267	22. 676 -17. 715	57. 171	1. 00 38. 87

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	ATOM	1999	0	ASP	267	21. 888 -18. 353	57. 867	1. 00 39. 64
	ATOM	2000	N	GLU	268	23. 879 -18. 179	56. 860	1. 00 38. 72
	ATOM	2001	CA	GLU	268	24. 301 -19. 502	57. 313	1. 00 39. 91
	ATOM	2002	CB	GLU	268	25. 510 -19. 971	56. 495	1. 00 40. 60
5	ATOM	2003	CG	GLU	268	26. 847 -19. 444	56. 976	1. 00 43. 85
	ATOM	2004	CD	GLU	268	27. 969 -19. 710	55. 981	1. 00 47. 64
	ATOM	2005	0E1	GLU	268	28. 013 -19. 017	54. 941	1. 00 49. 73
	ATOM	2006	0E2	GLU	268	28. 802 -20. 612	56. 232	1. 00 48. 40
	ATOM	2007	C	GLU	268	24. 633 -19. 577	58. 807	1. 00 40. 59
10	ATOM	2008	0	GLU	268	24. 790 -20. 667	59. 360	1. 00 41. 43
	ATOM	2009	N	PHE	269	24. 734 -18. 427	59. 462	1. 00 39. 17
	ATOM	2010	CA	PHE	269	25. 070 -18. 402	60. 882	1. 00 37. 75
	ATOM	2011	CB	PHE	269	26. 182 -17. 385	61. 127	1. 00 34. 69
	ATOM	2012	CG	PHE	269	27. 435 -17. 675	60. 369	1. 00 35. 74
15	ATOM	2013	CD1	PHE	269	28. 144 -18. 853	60. 599	1. 00 35. 94
	ATOM	2014	CD2	PHE	269	27. 910 -16. 781	59. 416	1. 00 34. 75
	ATOM	2015	CE1	PHE	269	29. 306 -19. 136	59. 891	1. 00 34. 71
	ATOM	2016	CE2	PHE	269	29. 068 -17. 050	58. 701	1. 00 34. 58
	ATOM	2017	CZ	PHE	269	29. 770 -18. 233	58. 939	1. 00 35. 80
20	ATOM	2018	C	PHE	269	23. 898 -18. 085	61. 793	1. 00 36. 73
	ATOM	2019	0	PHE	269	23. 932 -18. 384	62. 984	1. 00 36. 59
	ATOM	2020	N	LEU	270	22. 861 -17. 480	61. 231	1. 00 37. 18
	ATOM	2021	CA	LEU	270	21. 696 -17. 107	62. 012	1. 00 37. 71
	ATOM	2022	CB	LEU	270	20. 712 -16. 332	61. 135	1. 00 36. 52
25	ATOM	2023	CG	LEU	270	21. 264 -15. 036	60. 521	1. 00 37. 18
	ATOM	2024	CD1	LEU	270	20. 299 -14. 516	59. 466	1. 00 38. 72
	ATOM	2025	CD2	LEU	270	21. 488 -13. 990	61. 604	1. 00 34. 72
	MOTA	2026	С	LEU	270	21. 010 -18. 312	62. 644	1. 00 38. 27
	ATOM	2027	0	LEU	270	20. 794 -19. 333	61. 995	1. 00 39. 49

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	ATOM	2028	N	LEU	271	20. 685 -18. 176	63. 924	1. 00 37. 92
	ATOM	2029	CA	LEU	271	20. 010 -19. 212	64. 693	1. 00 38. 22
	ATOM	2030	CB	LEU	271	20. 657 -19. 339	66. 078	1. 00 37. 71
	ATOM	2031	CG	LEU	271	21. 897 -20. 220	66. 261	1. 00 38. 14
5	ATOM	2032	CD1	LEU	271	22. 827 -20. 111	65. 075	1. 00 39. 09
	ATOM	2033	CD2	LEU	271	22. 596 -19. 830	67. 549	1. 00 35. 73
	ATOM	2034	C	LEU	271	18. 536 -18. 845	64. 855	1. 00 39. 78
	ATOM	2035	0	LEU	271	18. 125 -17. 721	64. 538	1. 00 38. 05
	ATOM	2036	N	GLU	272	17. 751 -19. 794	65. 358	1. 00 39. 69
10	ATOM	2037	CA	GLU	272	16. 322 -19. 590	65. 575	1. 00 41. 03
	ATOM	2038	CB	GLU	272	15. 697 -20. 842	66. 219	1. 00 43. 64
	ATOM	2039	CG	GLU	272	16. 221 -21. 179	67. 627	1. 00 47. 44
	ATOM	2040	CD	GLU	272	15. 685 -22. 509	68. 182	1. 00 49. 81
	ATOM	2041	0E1 (GLU	272	16. 081 -23. 580	67. 666	1. 00 51. 29
15	ATOM	2042	0E2 (GLU	272	14. 869 -22. 484	69. 134	1. 00 47. 60
	ATOM	2043	C (GLU	272	16. 084 -18. 377	66. 466	1. 00 39. 89
	ATOM	2044	0 (GLU	272	15. 151 -17. 602	66. 250	1. 00 40. 35
	ATOM	2045	N 7	ryr	273	16. 944 -18. 208	67. 465	1. 00 38. 65
	ATOM	2046	CA 7	ΓYR	273	16. 813 -17. 095	68. 393	1. 00 35. 97
20	ATOM	2047	CB 7	TYR	273	17. 829 -17. 238	69. 530	1. 00 35. 50
	ATOM	2048	CG 1	TYR	273	18. 008 -18. 658	70. 009	1. 00 34. 45
	ATOM	2049	CD1 T	TYR	273	19. 109 -19. 416	69. 611	1. 00 32. 53
	ATOM	2050	CE1 T	YR	273	19. 252 -20. 740	70. 017	1. 00 35. 58
	ATOM	2051	CD2 T	YR	273	17. 053 -19. 258	70. 830	1. 00 34. 35
25	ATOM	2052	CE2 T	YR	273	17. 185 -20. 580	71. 241	1. 00 34. 82
	ATOM	2053	CZ T	'YR	273	18. 281 -21. 314	70. 830	1. 00 35. 96
	ATOM	2054	OH T	YR	273	18. 381 -22. 626	71. 208	1. 00 38. 31
	ATOM	2055	C T	YR	273	17. 021 -15. 763	67. 680	1. 00 35. 11
	ATOM	2056	0 T	YR	273	16. 404 -14. 752	68. 031	1. 00 34. 85

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	ATOM	2057	N	ASP	274	17. 888 -15. 763	66. 676	1. 00 36. 47
	ATOM	2058	CA	ASP	274	18. 164 -14. 541	65. 933	1. 00 36. 65
	ATOM	2059	CB	ASP	274	19. 405 -14. 718	65. 059	1. 00 32. 36
	ATOM	2060	CG	ASP	274	20. 627 -15. 072	65. 869	1. 00 32. 89
5	ATOM	2061	OD 1	ASP	274	20. 949 -14. 315	66. 810	1. 00 30. 53
	ATOM	2062	OD2	ASP	274	21. 265 -16. 104	65. 569	1. 00 32. 08
	ATOM	2063	C	ASP	274	16. 968 -14. 165	65. 081	1. 00 37. 27
	ATOM	2064	0	ASP	274	16. 571 -13. 001	65. 040	1. 00 37. 20
	ATOM	2065	N	ARG	275	16. 380 -15. 148	64. 410	1. 00 39. 32
10	ATOM	2066	CA	ARG	275	15. 222 -14. 866	63. 574	1. 00 41. 70
	ATOM	2067	CB	ARG	275	14. 803 -16. 121	62. 809	1. 00 44. 47
	ATOM	2068	CG	ARG	275	15. 908 -16. 666	61. 914	1. 00 49. 05
	ATOM	2069	CD	ARG	275	15. 516 -18. 002	61. 303	1. 00 53. 46
	ATOM	2070	NE	ARG	275	16. 668 -18. 740	60. 779	1. 00 57. 36
15	ATOM	2071	CZ	ARG	275	17. 352 -18. 408	59. 685	1. 00 58. 81
	ATOM	2072	NH1	ARG	275	18. 383 -19. 148	59. 296	1. 00 60. 43
	ATOM	2073	NH2	ARG	275	17. 005 -17. 341	58. 976	1. 00 61. 75
	ATOM	2074	C	ARG	275	14. 079 -14. 353	64. 446	1. 00 41. 43
	ATOM	2075	0	ARG	275	13. 350 -13. 444	64. 059	1. 00 40. 04
20	ATOM	2076	N	LEU	276	13. 939 -14. 927	65. 637	1. 00 40. 97
	ATOM	2077	CA	LEU	276	12. 888 -14. 507	66. 556	1. 00 42. 14
	ATOM	2078	CB	LEU	276	12. 831 -15. 450	67. 761	1. 00 44. 12
	ATOM	2079	CG	LEU	276	12. 315 -16. 862	67. 468	1. 00 47. 86
	ATOM	2080	CD1	LEU	276	12. 662 -17. 800	68. 618	1. 00 48. 62
25	ATOM	2081	CD2	LEU	276	10. 808 -16. 808	67. 236	1. 00 47. 43
	ATOM	2082	C	LEU	276	13. 094 -13. 072	67. 034	1. 00 40. 87
	ATOM	2083	0	LEU	276	12. 152 -12. 281	67. 072	1. 00 41. 20
	ATOM	2084	N	VAL	277	14. 322 -12. 740	67. 412	1. 00 39. 68
	ATOM	2085	CA	VAL	277	14. 617 -11. 390	67. 876	1. 00 40. 86

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	ATOM	2086	CB	VAL	277	16. 084 -11. 263	68. 331	1. 00 41. 86
	ATOM	2087	CG1	VAL	277	16. 447 -9. 802	68. 497	1. 00 43. 25
	ATOM	2088	CG2	VAL	277	16. 290 -12. 012	69. 647	1. 00 41. 47
	ATOM	2089	C	VAL	277	14. 363 -10. 381	66. 761	1. 00 40. 10
5	ATOM	2090	0	VAL	277	13. 813 -9. 305	66. 993	1. 00 41. 12
	ATOM	2091	N	ASP	278	14. 767 -10. 738	65. 550	1. 00 39. 42
	ATOM	2092	CA	ASP	278	14. 592 -9. 867	64. 398	1. 00 40. 24
	ATOM	2093	CB	ASP	278	15. 356 -10. 434	63. 195	1. 00 38. 24
	ATOM	2094	CG	ASP	278	15. 179 -9. 598	61. 943	1. 00 40. 23
10	ATOM	2095	OD 1	ASP	278	15. 260 -8. 351	62. 043	1. 00 39. 72
	ATOM	2096	OD2	ASP	278	14. 969 -10. 187	60. 860	1. 00 38. 10
	ATOM	2097	C	ASP	278	13. 120 -9. 669	64. 043	1. 00 41. 19
	ATOM	2098	0	ASP	278	12. 693 -8. 545	63. 791	1. 00 40. 82
	ATOM	2099	N	GLU	279	12. 347 -10. 754	64. 035	1. 00 43. 34
15	ATOM	2100	CA	GLU	279	10. 922 -10. 688	63. 696	1. 00 46. 81
	ATOM	2101	CB	GLU	279	10. 321 -12. 097	63. 627	1. 00 50. 53
	ATOM	2102	CG	GLU	279	10. 870 -12. 965	62. 496	1. 00 56. 10
	ATOM	2103	CD	GLU	279	10. 320 -14. 382	62. 523	1. 00 59. 07
	ATOM	2104	0E1	GLU	279	10. 336 -15. 006	63. 607	1. 00 60. 28
20	ATOM	2105	0E2	GLU	279	9. 880 -14. 876	61. 461	1. 00 60. 79
	ATOM	2106	C	GLU	279	10. 086 -9. 840	64. 652	1. 00 47. 25
	ATOM	2107	0	GLU	279	9. 048 -9. 303	64. 260	1. 00 46. 34
	ATOM	2108	N	SER	280	10. 535 -9. 722	65. 899	1. 00 46. 87
	ATOM	2109	CA	SER	280	9. 809 -8. 948	66. 900	1. 00 47. 53
25	ATOM	2110	CB	SER	280	9. 769 -9. 708	68. 228	1. 00 49. 98
	ATOM	2111	0G	SER	280	9. 043 -10. 919	68. 093	1. 00 52. 36
	ATOM	2112	C	SER	280	10. 415 -7. 575	67. 129	1. 00 47. 33
	ATOM	2113	0	SER	280	9. 909 -6. 788	67. 936	1. 00 45. 86
	ATOM	2114	N	SER	281	11. 499 -7. 289	66. 416	1. 00 46. 95

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	ATOM	2115	CA	SER	281	12. 172	-6. 004	66. 552	1. 00	46. 75
	ATOM	2116	CB	SER	281	13. 581	-6. 081	65. 971	1. 00	47. 24
	ATOM	2117	0G	SER	281	13. 524	-6. 172	64. 559	1. 00	47. 80
	ATOM	2118	C	SER	281	11. 391	-4. 915	65. 824	1. 00	45. 65
5	ATOM	2119	0	SER	281	10. 514	-5. 199	65. 013	1. 00	45. 10
	ATOM	2120	N	ALA	282	11. 723	-3. 667	66. 123	1. 00	45. 75
	ATOM	2121	CA	ALA	282	11.066	-2. 530	65. 500	1. 00	45. 70
	ATOM	2122	CB	ALA	282	11. 257	-1. 289	66. 354	1. 00	45. 60
	ATOM	2123	C	ALA	282	11. 617	-2. 286	64. 100	1. 00	46. 48
10	ATOM	2124	0	ALA	282	11. 252	-1. 303	63. 449	1. 00	48. 61
	ATOM	2125	N	ASN	283	12. 493	-3. 172	63. 633	1. 00	43. 90
	ATOM	2126	CA	ASN	283	13. 076	-3. 015	62. 306	1. 00	41. 45
	ATOM	2127	CB	ASN	283	14. 300	-2. 092	62. 384	1. 00	40. 08
	ATOM	2128	CG	ASN	283	15. 398	-2. 631	63. 289	1. 00	39. 25
15	ATOM	2129	0D1	ASN	283	15. 136	-3. 308	64. 289	1. 00	37. 65
	MOTA	2130	ND2	ASN	283	16. 641	-2. 310	62. 950	1. 00	37. 96
	ATOM	2131	C	ASN	283	13. 433	-4. 350	61. 655	1. 00	41.06
	ATOM	2132	0	ASN	283	14. 585	-4. 606	61. 318	1. 00	40. 48
	ATOM	2133	N	PR0	284	12. 423	-5. 211	61. 455	1. 00	40. 23
20	ATOM	2134	CD	PR0	284	11. 013	-4. 898	61. 751	1. 00	40. 75
	ATOM	2135	CA	PR0	284	12. 534	-6. 540	60. 851	1. 00	40. 08
	ATOM	2136	CB	PRO	284	11. 080	-6. 914	60. 581	1. 00	40. 52
	ATOM	2137	CG	PR0	284	10. 364	-6. 260	61. 712	1. 00	41. 21
	ATOM	2138	C	PR0	284	13. 366	-6. 565	59. 579	1. 00	39. 55
25	ATOM	2139	0	PRO	284	13. 054	-5. 868	58. 617	1. 00	40. 95
	ATOM	2140	N	GLY	285	14. 416	-7. 382	59. 576	1. 00	38. 56
	ATOM	2141	CA	GLY	285	15. 266	-7. 491	58. 407	1. 00	35. 73
	ATOM	2142	C	GLY	285	16. 428	-6. 516	58. 371	1. 00	35. 10
	ATOM	2143	0	GLY '	285	17. 288	-6. 624	57. 500	1. 00	36. 22

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	ATOM	2144	N	GLN	286	16. 468	-5. 573	59. 308	1. 00 34. 06
	ATOM	2145	CA	GLN	286	17. 547	-4. 584	59. 348	1. 00 34. 96
	ATOM	2146	CB	GLN	286	16. 974	-3. 166	59. 321	1. 00 39. 16
	ATOM	2147	CG	GLN	286	16. 189	-2. 825	58. 067	1. 00 45. 72
5	ATOM	2148	CD	GLN	286	15. 698	-1. 384	58. 074	1. 00 51. 15
	ATOM	2149	0E1	GLN	286	14. 816	-1. 018	58. 860	1. 00 52. 21
	ATOM	2150	NE2	GLN	286	16. 276	-0. 555	57. 203	1. 00 50. 85
	ATOM	2151	C	GLN	286	18. 439	-4. 719	60. 573	1. 00 33. 59
	ATOM	2152	0	GLN	286	17. 993	-5. 157	61. 637	1. 00 33. 18
10	ATOM	2153	N	GLN	287	19. 701	-4. 334	60. 408	1. 00 32. 85
	ATOM	2154	CA	GLN	287	20. 691	-4. 375	61. 484	1. 00 32. 45
	ATOM	2155	CB	GLN	287	20. 248	-3. 456	62. 636	1. 00 33. 34
	ATOM	2156	CG	GLN	287	19. 955	-1. 999	62. 251	1. 00 31. 48
	ATOM	2157	CD	GLN	287	21. 188	-1. 259	61. 743	1. 00 31. 78
15	ATOM	2158	0E1	GLN	287	21. 330	-1. 010	60. 544	1. 00 33. 25
	ATOM	2159	NE2	GLN	287	22. 090	-0. 921	62. 652	1. 00 27. 51
	ATOM	2160	C	GLN	287	20. 924	-5. 788	62. 032	1. 00 30. 79
	ATOM	2161	0	GLN	287	21. 120	-5. 957	63. 229	1. 00 29. 31
	ATOM	2162	N	LEU	288	20. 921	-6. 791	61. 158	1. 00 29. 33
20	ATOM	2163	CA	LEU	288	21. 101	-8. 181	61. 585	1. 00 27. 53
	ATOM	2164	CB	LEU	288	20. 940	-9. 129	60. 393	1. 00 28. 13
	ATOM	2165	CG	LEU	288	19. 599	-9. 090	59. 647	1. 00 29. 14
	ATOM	2166	CD1	LEU	288	19. 390	-10. 418	58. 922	1. 00 27. 60
	ATOM	2167	CD2	LEU	288	18. 453	-8. 844	60. 621	1. 00 27. 42
25	ATOM	2168	C	LEU	288	22. 418	-8. 476	62. 297	1. 00 27. 92
	ATOM	2169	0	LEU	288	22. 438	-9. 184	63. 303	1. 00 28. 24
	ATOM	2170	N	TYR	289	23. 520	-7. 946	61. 776	1. 00 27. 17
	ATOM	2171		TYR	289	24. 819	-8. 153	62. 399	1. 00 24. 83
	ATOM	2172	CB	TYR	289	25. 899	-7. 458	61. 583	1. 00 24. 32

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	ATOM	2173	CG	TYR	289	27. 303	-7. 575	62. 137	1. 00	21. 26
	ATOM	2174	CD1	TYR	289	27. 951	-8. 814	62. 208	1. 00	20.00
	ATOM	2175	CE1	TYR	289	29. 281	-8. 909	62. 616	1. 00	18. 43
	ATOM	2176	CD2	TYR	289	28. 013	-6. 441	62. 503	1. 00	18. 12
5	ATOM	2177	CE2	TYR	289	29. 338	-6. 520	62. 918	1. 00	20. 65
	ATOM	2178	CZ	TYR	289	29. 976	-7. 762	62. 966	1. 00	21. 27
	ATOM	2179	ОН	TYR	289	31. 314	-7. 833	63. 326	1. 00	19. 02
	ATOM	2180	C	TYR	289	24. 771	-7. 566	63. 799	1. 00	26. 94
	ATOM	2181	0	TYR	289	25. 221	-8. 175	64. 776	1. 00	27. 95
10	ATOM	2182	N	GLU	290	24. 198	-6. 374	63. 892	1. 00	27. 68
	ATOM	2183	CA	GLU	290	24. 078	-5. 686	65. 165	1. 00	26. 41
	ATOM	2184	CB	GLU	290	23. 484	-4. 309	64. 927	1. 00	26. 55
	ATOM	2185	CG	GLU	290	23. 059	-3. 595	66. 180	1. 00	27. 05
	ATOM	2186	CD	GLU	290	22. 815	-2. 142	65. 913	1. 00	25. 47
15	ATOM	2187	0E1	GLU	290	23. 716	-1. 336	66. 204	1. 00	27. 17
	ATOM	2188	0E2	GLU	290	21. 731	-1. 815	65. 398	1. 00	29. 09
	ATOM	2189	C	GLU	290	23. 218	-6. 463	66. 159	1. 00	26. 59
	ATOM	2190	0	GLU	290	23. 458	-6. 430	67. 371	1. 00	25. 62
	ATOM	2191	N	LYS	291	22. 216	-7. 166	65. 646	1. 00	26. 31
20	ATOM	2192	CA	LYS	291	21. 343	-7. 942	66. 509	1. 00	27. 77
	ATOM	2193	CB	LYS	291	20. 110	-8. 394	65. 722	1. 00	28. 30
	ATOM	2194	CG	LYS	291	19. 096	-7. 263	65. 585	1. 00	33, 35
	ATOM	2195	CD	LYS	291	18. 005	-7. 529	64. 555	1. 00	33. 56
	ATOM	2196	CE	LYS	291	17. 038	-6. 330	64. 522	1. 00	36. 46
25	ATOM	2197	NZ	LYS	291	16. 150	-6. 319	63. 327	1. 00	36. 55
	ATOM	2198	C	LYS	291	22. 073	-9. 123	67. 138	1. 00	26. 53
	ATOM	2199	0	LYS	291	21. 584	-9. 736	68. 084	1. 00	27. 81
	ATOM	2200	N	LEU	292	23. 261	-9. 426	66. 628	1. 00	26. 02
	ATOM	2201	CA	LEU	292	24. 043	-10. 523	67. 168	1. 00	25. 35

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	ATOM	2202	СВ	LEU	292	24. 922	-11, 140	66 079	1. 00 25. 16
	ATOM	2203	CG	LEU	292				1. 00 26. 25
	ATOM	2204	CD	1 LEU	292				1. 00 23. 09
	ATOM	2205		2 LEU	292		-12. 912		
5	ATOM	2206	С	LEU	292		-10. 030		
	ATOM	2207	0	LEU	292		-10. 808		
	ATOM	2208	N	ILE	293		-8. 723		
	ATOM	2209	CA	ILE	293		-8. 140		1. 00 23. 59
	ATOM	2210	CB	ILE	293	27. 259			
10	ATOM	2211	CG2	2 ILE	293	28. 233	-6. 762		
	ATOM	2212	CG1	ILE	293	27. 952	-8. 527		
	ATOM	2213	CD1	ILE	293	28. 715	-7. 965	66. 441	1. 00 25. 64
	ATOM	2214	C	ILE	293	25. 560	-7. 148	70. 278	1. 00 25. 10
	ATOM.	2215	0	ILE	293	25. 797	-7. 289	71. 474	1. 00 23. 79
15	ATOM	2216	N	GLY	294	24. 845	-6. 136	69. 781	1. 00 28. 83
	ATOM	2217	CA	GLY	294	24. 302	-5. 071	70. 615	1. 00 26. 73
	ATOM	2218	C	GLY	294	23. 551	-5. 379	71. 898	1. 00 29. 79
	ATOM	2219	0	GLY	294	22. 757	-6. 318	71. 964	1. 00 27. 85
	ATOM	2220	N	GLY	295	23. 794	-4. 553	72. 918	1. 00 30. 56
20	ATOM	2221	CA	GLY	295	23. 136	-4. 722	74. 204	1. 00 33. 01
	ATOM	2222	C	GLY	295	21. 628	-4. 539	74. 144	1. 00 34. 05
	ATOM	2223	0	GLY	295	20. 927	-4. 810	75. 107	1. 00 34. 93
	ATOM	2224	N	LYS	296	21. 124	-4. 058	73. 016	1. 00 35. 19
	ATOM	2225	CA	LYS	296	19. 690	-3. 868	72. 851	1. 00 36. 24
25	ATOM	2226	CB	LYS	296	19. 419	-2. 988	71. 626	1. 00 38. 05
	ATOM	2227	CG	LYS	296	17. 961	-2. 910	71. 181	1. 00 40. 26
	ATOM	2228	CD	LYS	296	17. 122	-2. 093	72. 141	1. 00 43. 32
	ATOM	2229	CE	LYS	296	15. 730	-1. 862	71. 579	1. 00 44. 42
	ATOM	2230	NZ	LYS	296	14. 842	-1. 175	72. 562	1. 00 44. 77

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	ATOM	2231	С	LYS	296	19. 045	-5. 235	72. 654	1. 00	36. 63
	ATOM	2232	0	LYS	296	17. 867	-5. 420	72. 963	1. 00	38. 56
	ATOM	2233	N	TYR	297	19. 836	-6. 193	72. 168	1. 00	34. 63
	ATOM	2234	CA	TYR	297	19. 346	-7. 539	71. 890	1. 00	33. 22
5	ATOM	2235	CB	TYR	297	19. 487	-7.810	70. 389	1. 00	34. 65
	ATOM	2236	CG	TYR	297	19. 073	-6. 631	69. 535	1. 00	36. 28
	ATOM	2237	CD1	TYR	297	20. 010	-5. 677	69. 125	1. 00	34. 21
	ATOM	2238	CE1	TYR	297	19. 622	-4. 548	68. 404	1. 00	36. 22
	ATOM	2239	CD2	TYR	297	17. 732	-6. 431	69. 195	1. 00	34. 24
10	ATOM	2240	CE2	TYR	297	17. 330	-5. 305	68. 476	1. 00	35. 71
	ATOM	2241	CZ	TYR	297	18. 280	-4. 368	68. 082	1. 00	37. 38
	ATOM	2242	ОН	TYR	297	17. 887	-3. 258	67. 375	1. 00	35. 33
	ATOM	2243	C	TYR	297	19. 968	-8. 713	72. 670	1. 00	33. 21
	ATOM	2244	0	TYR	297	19. 392	-9. 800	72. 716	1. 00	33. 78
15	ATOM	2245	N	MET	298	21. 126	-8. 504	73. 283	1.00	31. 19
	ATOM	2246	CA	MET	298	21. 803	-9. 576	74. 005	1. 00	30. 16
	ATOM	2247	CB	MET	298	23. 075	-9. 038	74. 644	1. 00	30. 05
	ATOM	2248	CG	MET	298	23. 957	-10. 104	75. 231	1. 00	26. 86
	ATOM	2249	SD	MET	298	25. 486	-9. 405	75. 850	1. 00	32. 83
20	ATOM	2250	CE	MET	298	26. 409	-9. 201	74. 338	1. 00	29. 59
	ATOM	2251	C	MET	298	20. 963	-10. 296	75. 066	1. 00	31. 27
	ATOM	2252	0	MET	298	20. 882	-11. 529	75. 077	1. 00	29. 78
	ATOM	2253	N	GLY	299	20. 353	-9. 530	75. 963	1. 00	30. 40
	ATOM	2254	CA	GLY	299	19. 534	-10. 132	76. 998	1. 00	31. 32
25	ATOM	2255	C	GLY	299	18. 354	-10. 869	76. 393	1. 00	33. 32
	ATOM	2256	0	GLY	299	17. 988	-11. 962	76. 831	1. 00	33. 97
	ATOM	2257	N	GLU	300	17. 752	-10. 265	75. 377	1. 00	31. 78
	ATOM	2258	CA	GLU	300	16. 617	-10. 874	74. 707	1. 00	31. 93
	ATOM	2259	CB	GLU	300	16. 080	-9. 937	73. 621	1. 00	29. 00

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	ATOM	2260	CG	GLU	300	14. 877 -10. 486	72. 881	1. 00 32. 60
	ATOM	2261	CD	GLU	300	13. 655 -10. 655	73. 769	1. 00 31. 13
	ATOM	2262	0E1	GLU	300	12. 629 -11. 144	73. 265	1. 00 34. 55
	ATOM	2263	0E2	GLU	300	13. 714 -10. 299	74. 963	1. 00 33. 16
5	ATOM	2264	C	GLU	300	17. 013 -12. 215	74. 092	1. 00 30. 90
	ATOM	2265	0	GLU	300	16. 225 -13. 156	74. 090	1. 00 32. 89
	ATOM	2266	N	LEU	301	18. 234 -12. 301	73. 570	1. 00 31. 16
	ATOM	2267	CA	LEU	301	18. 714 -13. 546	72. 973	1. 00 28. 93
	ATOM	2268	CB	LEU	301	20. 085 -13. 339	72. 325	1. 00 24. 69
10	ATOM	2269	CG	LEU	301	20. 152 -12. 667	70. 952	1. 00 24. 17
	ATOM	2270	CD1	LEU	301	21. 607 -12. 326	70. 628	1. 00 23. 70
	ATOM	2271	CD2	LEU	301	19. 560 -13. 598	69. 886	1. 00 23. 13
	ATOM	2272	C	LEU	301	18. 814 -14. 616	74. 056	1. 00 29. 42
	ATOM	2273	0	LEU	301	18. 408 -15. 761	73. 853	1. 00 32. 03
15	ATOM	2274	N	VAL	302	19. 365 -14. 239	75. 204	1. 00 28. 73
	ATOM	2275	CA	VAL	302	19. 505 -15. 164	76. 317	1. 00 29. 42
	ATOM	2276	CB	VAL	302	20. 265 -14. 510	77. 497	1. 00 26. 51
	ATOM	2277	CG1	VAL	302	20. 172 -15. 395	78. 740	1. 00 25. 63
	ATOM	2278	CG2	VAL	302	21. 731 -14. 301	77. 117	1. 00 25. 98
20	ATOM	2279	C	VAL	302	18. 127 -15. 624	76. 795	1. 00 31. 88
	ATOM	2280	0	VAL	302	17. 934 -16. 795	77. 112	1. 00 32. 71
	ATOM	2281	N	ARG	303	17. 171 -14. 703	76. 835	1. 00 32. 91
	ATOM	2282	CA	ARG	303	15. 818 -15. 039	77. 270	1. 00 36. 08
	ATOM	2283	CB	ARG	303	14. 910 -13. 802	77. 250	1. 00 35. 86
25	ATOM	2284	CG	ARG	303	13. 524 -14. 055	77. 847	1. 00 36. 97
	ATOM	2285	CD	ARG	303	12. 660 -12. 802	77. 833	1. 00 39. 15
	ATOM	2286	NE	ARG	303	12. 105 -12. 529	76. 511	1. 00 41. 95
	MOTA	2287	CZ	ARG	303	11. 090 -13. 197	75. 968	1. 00 43. 84
	ATOM	2288	NH1	ARG	303	10. 502 -14. 182	76. 631	1. 00 42. 47

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	ATOM	2289	NH2	ARG	303	10. 666 -12. 885	74. 750	1. 00 43. 86
	ATOM	2290	C	ARG	303	15. 215 -16. 110	76. 373	1. 00 36. 97
	ATOM	2291	0	ARG	303	14. 554 -17. 032	76. 851	1. 00 37. 22
	ATOM	2292	N	LEU	304	15. 432 -15. 970	75. 068	1. 00 37. 86
5	ATOM	2293	CA	LEU	304	14. 914 -16. 924	74. 103	1. 00 37. 63
	ATOM	2294	CB	LEU	304	15. 113 -16. 387	72. 687	1. 00 38. 69
	ATOM	2295	CG	LEU	304	13. 944 -15. 590	72. 104	1. 00 40. 35
	ATOM	2296	CD1	LEU	304	13. 486 -14. 516	73. 062	1. 00 40. 85
	ATOM	2297	CD2	LEU	304	14. 378 `-14. 986	70. 785	1. 00 42. 07
10	ATOM	2298	C	LEU	304	15. 602 -18. 272	74. 262	1. 00 37. 69
	ATOM	2299	0	LEU	304	14. 978 -19. 324	74. 120	1. 00 38. 84
	ATOM	2300	N	VAL	305	16. 893 -18. 238	74. 558	1. 00 36. 28
	ATOM	2301	CA	VAL	305	17. 647 -19. 466	74. 753	1. 00 34. 31
	ATOM	2302	CB	VAL	305	19. 148 -19. 184	74. 908	1. 00 32. 24
15	ATOM	2303	CG1	VAL	305	19. 868 -20. 438	75. 390	1. 00 28. 85
	ATOM	2304	CG2	VAL	305	19. 717 -18. 713	73. 578	1. 00 29. 80
	ATOM	2305	C	VAL	305	17. 153 -20. 158	76. 012	1. 00 35. 48
	ATOM	2306	.0 .	VAL	305	17. 079 -21. 389	76. 070	1. 00 34. 47
	ATOM	2307	N	LEU	306	16. 820 -19. 362	77. 023	1. 00 34. 14
20	ATOM	2308	CA	LEU	306	16. 328 -19. 921	78. 273	1. 00 35. 52
	ATOM	2309	CB	LEU	306	16. 257 -18. 841	79. 353	1. 00 32. 11
	ATOM	2310	CG	LEU	306	17. 601 -18. 289	79. 829	1. 00 32. 53
	ATOM	2311	CD1	LEU	306	17. 359 -17. 326	80. 964	1. 00 33. 54
	ATOM	2312	CD2	LEU	306	18. 515 -19. 420	80. 287	1. 00 30. 60
25	ATOM	2313	С	LEU	306	14. 948 -20. 532	78. 049	1. 00 37. 53
	ATOM	2314	0	LEU	306	14. 637 -21. 608	78. 566	1. 00 33. 87
	ATOM	2315	N	LEU	307	14. 129 -19. 850	77. 257	1. 00 39. 39
	ATOM	2316	CA	LEU	307	12. 787 -20. 336	76. 971	1. 00 41. 43
	ATOM	2317	CB	LEU	307	12. 011 -19. 296	76. 165	1. 00 40. 84

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	ATOM	2318	CG	LEU	307	10. 932 -18. 527	76. 935	1. 00 43. 43
	ATOM	2319	CD1	LEU	307	11. 389 -18. 243	78. 356	1. 00 43. 36
	ATOM	2320	CD2	LEU	307	10. 610 -17. 233	76. 197	1. 00 41. 75
	ATOM	2321	C	LEU	307	12. 802 -21. 674	76. 239	1. 00 42. 39
5	ATOM	2322	0	LEU	307	11. 974 -22. 537	76. 514	1. 00 42. 90
	ATOM	2323	N	ARG	308	13. 729 -21. 860	75. 306	1. 00 42. 02
	ATOM	2324	CA	ARG	308	13. 771 -23. 132	74. 605	1. 00 42. 88
	ATOM	2325	CB	ARG	308	14. 765 -23. 125	73. 445	1. 00 43. 55
	ATOM	2326	CG	ARG	308	14. 891 -24. 514	72. 837	1. 00 47. 00
10	ATOM	2327	CD	ARG	308	15. 908 -24. 626	71. 729	1. 00 49. 25
	ATOM	2328	NE	ARG	308	16. 079 -26. 026	71. 349	1. 00 52. 10
	ATOM	2329	CZ	ARG	308	16. 915 -26. 456	70. 410	1. 00 52. 45
	ATOM	2330	NH1	ARG	308	17. 663 -25. 591	69. 739	1. 00 54. 77
	ATOM	2331	NH2	ARG	308	17. 016 -27. 756	70. 154	1. 00 51. 73
15	ATOM	2332	C	ARG	308	14. 181 -24. 222	75. 582	1. 00 43. 27
	ATOM	2333	0	ARG	308	13. 654 -25. 333	75. 540	1. 00 42. 09
	ATOM	2334	N	LEU	309	15. 135 -23. 895	76. 452	1. 00 42. 54
	ATOM	2335	CA	LEU	309	15. 627 -24. 837	77. 447	1. 00 42. 29
	ATOM	2336	CB	LEU	309	16. 771 -24. 207	78. 248	1. 00 40. 55
20	ATOM	2337	CG	LEU	309	18. 193 -24. 656	77. 886	1. 00 39. 65
	ATOM	2338	CD1	LEU	309	18. 313 -24. 973	76. 416	1. 00 38. 56
	ATOM	2339	CD2	LEU	309	19. 171 -23. 569	78. 284	1. 00 37. 67
	ATOM	2340	C	LEU	309	14. 515 -25. 302	78. 379	1. 00 42. 66
	ATOM	2341	0	LEU	309	14. 509 -26. 450	78. 818	1. 00 41. 33
25	ATOM	2342	N	VAL	310	13. 570 -24. 416	78. 676	1. 00 44. 27
	ATOM	2343	CA	VAL	310	12. 464 -24. 789	79. 543	1. 00 46. 40
	ATOM	2344	CB	VAL	310	11. 711 -23. 546	80. 111	1. 00 46. 06
	ATOM	2345	CG1	VAL	310	12. 682 -22. 613	80. 807	1. 00 45. 43
	ATOM	2346	CG2	VAL	310	10. 976 -22. 825	79. 014	1. 00 48. 29

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	ATOM	2347	C	VAL	310	11. 479 -25. 666	78. 769	1. 00 48. 00
	ATOM	2348	0	VAL	310	10. 952 -26. 638	79. 311	1. 00 47. 71
	ATOM	2349	N	ASP	311	11. 242 -25. 333	77. 501	1. 00 49. 58
	ATOM	2350	CA	· ASP	311	10. 313 -26. 104	76. 683	1. 00 52. 37
5	ATOM	2351	CB	ASP	311	9. 978 -25. 365	75. 382	1. 00 54. 70
	ATOM	2352	CG	ASP	311	9. 318 -24. 014	75. 626	1. 00 58. 89
	ATOM	2353	OD1	ASP	311	8. 742 -23. 808	76. 719	1. 00 60. 74
	ATOM	2354	OD2	ASP	311	9. 364 -23. 158	74. 713	1. 00 60. 54
	ATOM	2355	C	ASP	311	10. 872 -27. 485	76. 365	1. 00 52. 35
10	ATOM	2356	0	ASP	311	10. 131 -28. 388	75. 982	1. 00 55. 07
	ATOM	2357	N	GLU	312	12. 180 -27. 642	76. 515	1. 00 51. 23
	ATOM	2358	CA	GLU	312	12. 828 -28. 926	76. 279	1. 00 51. 12
	ATOM	2359	CB	GLU	312	14. 277 -28. 729	75. 834	1. 00 52. 62
	ATOM	2360	CG	GLU	312	14. 445 -28. 141	74. 448	1. 00 57. 13
15	ATOM	2361	CD	GLU	312	14. 187 -29. 153	73. 358	1. 00 58. 40
	MOTA	2362	0E1	GLU	312	14. 831 -30. 222	73. 385	1. 00 59. 31
	ATOM	2363	OE2	GLU	312	13. 346 -28. 879	72. 476	1. 00 60. 41
	ATOM	2364	C	GLU	312	12. 810 -29. 660	77. 611	1. 00 50. 76
	ATOM	2365	0	GLU	312	13. 292 -30. 787	77. 720	1. 00 50. 64
20	ATOM	2366	N	ASN	313	12. 265 -28. 989	78. 624	1. 00 50. 08
	ATOM	2367	CA	ASN	313	12. 154 -29. 533	79. 974	1. 00 51. 37
	ATOM	2368	CB	ASN	313	11. 428 -30. 886	79. 932	1. 00 53. 51
	ATOM	2369	CG	ASN	313	10. 846 -31. 275	81. 271	1. 00 55. 73
	ATOM	2370	OD1	ASN	313	10. 011 -30. 560	81. 824	1. 00 58. 95
25	ATOM	2371	ND2	ASN	313	11. 281 -32. 415	81. 803	1. 00 59. 16
	ATOM	2372	C	ASN	313	13. 524 -29. 693	80. 635	1. 00 50. 00
	ATOM	2373	0	ASN	313	13. 733 -30. 595	81. 447	1. 00 50. 40
	ATOM	2374	N	LEU	314	14. 449 -28. 799	80. 296	1. 00 48. 35
	ATOM	2375	CA	LEU	314	15. 805 -28. 843	80. 835	1. 00 45. 12

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	ATOM	2376	CB	LEU	314	16. 819 -28. 785	79. 688	1. 00 44. 25
	ATOM	2377	CG	LEU	314	16. 759 -29. 872	78. 611	1. 00 45. 98
	ATOM	2378	CD1	LEU	314	17. 619 -29. 465	77. 416	1. 00 43. 63
	ATOM	2379	CD2	LEU	314	17. 232 -31. 201	79. 196	1. 00 45. 09
5	ATOM	2380	C	LEU	314	16. 119 -27. 724	81. 829	1. 00 43. 38
	ATOM	2381	0	LEU	314	17. 180 -27. 732	82. 449	1. 00 41. 90
	ATOM	2382	N	LEU	315	15. 211 -26. 765	81. 982	1. 00 41. 74
	ATOM	2383	CA	LEU	315	15. 446 -25. 645	82. 899	1. 00 42. 39
	ATOM	2384	CB	LEU	315	15. 907 -24. 407	82. 116	1. 00 40. 17
10	ATOM	2385	CG	LEU	315	17. 243 -23. 721	82. 428	1. 00 39. 81
	ATOM	2386	CD1	LEU	315	17. 262 -22. 383	81. 689	1. 00 41. 89
	ATOM	2387	CD2	LEU	315	17. 421 -23. 482	83. 920	1. 00 37. 58
	ATOM	2388	C	LEU	315	14. 198 -25. 278	83. 694	1. 00 42. 28
	ATOM	2389	0	LEU	315	13. 103 -25. 214	83. 144	1. 00 40. 83
15	ATOM	2390	N	PHE	316	14. 377 -25. 021	84. 986	1. 00 43. 70
	ATOM	2391	CA	PHE	316	13. 271 -24. 648	85. 863	1. 00 46. 70
	ATOM	2392	CB	PHE	316	12. 717 -23. 278	85. 459	1. 00 47. 06
	ATOM	2393	CG	PHE	316	13. 776 -22. 247	85. 187	1. 00 47. 07
	ATOM _.	2394	CD1	PHE	316	14. 824 -22. 051	86. 082	1. 00 47. 24
20	ATOM	2395	CD2	PHE	316	13. 722 -21. 467	84. 037	1. 00 47. 25
	ATOM	2396	CE1	PHE	316	15. 803 -21. 094	85. 835	1. 00 46. 12
	ATOM	2397	CE2	PHE	316	14. 695 -20. 507	83. 782	1. 00 47. 70
	ATOM	2398	CZ	PHE	316	15. 738 -20. 321	84. 683	1. 00 47. 68
	ATOM	2399	С	PHE	316	12. 131 -25. 672	85. 857	1. 00 48. 45
25	ATOM	2400	0	PHE	316	10. 960 -25. 306	85. 967	1. 00 48. 86
	ATOM	2401	N	HIS	317	12. 473 -26. 950	85. 725	1. 00 50. 80
	ATOM	2402	CA	HIS	317	11. 469 -28. 009	85. 712	1. 00 53. 83
	ATOM	2403	CB	HIS	317	10. 655 -27. 986	87. 010	1. 00 57. 67
	ATOM	2404	CG	HIS	317	11. 496 -27. 985	88. 246	1. 00 61. 10

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	ATOM	2405	CD2	2 HIS	317	11. 558 -27. 116	89. 282	1. 00 63. 07
	ATOM	2406	ND 1	HIS	317	12. 430 -28. 965	88. 509	1. 00 62. 35
	ATOM	2407	CE	HIS	317	13. 032 -28. 699	89. 655	1. 00 64. 77
	ATOM	2408	NE	HIS	317	12. 521 -27. 582	90. 144	1. 00 65. 99
5	ATOM	2409	C	HIS	317	10. 521 -27. 859	84. 534	1. 00 53. 57
	ATOM	2410	0	HIS	317	9. 429 -28. 425	84. 537	1. 00 53. 60
	ATOM	2411	N	GLY	318	10. 939 -27. 090	83. 534	1. 00 52. 50
	ATOM	2412	CA	GLY	318	10. 113 -26. 881	82. 358	1. 00 51. 83
	ATOM	2413	C	GLY	318	8. 940 -25. 958	82. 615	1. 00 51. 72
10	ATOM	2414	0	GLY	318	7. 939 -25. 999	81. 904	1. 00 50. 88
	ATOM	2415	N	GLU	319	9. 073 -25. 110	83. 627	1. 00 53. 43
	ATOM	2416	CA	GLU	319	8. 014 -24. 182	83. 996	1. 00 55. 73
	ATOM	2417	CB	GLU	319	7. 510 -24. 544	85. 392	1. 00 58. 85
	ATOM	2418	CG	GLU	319	6. 145 -23. 998	85. 761	1. 00 63. 60
15	ATOM	2419	CD	GLU	319	5. 590 -24. 664	87. 016	1. 00 66. 32
	ATOM	2420	0E1	GLU	319	6. 206 -24. 527	88. 100	1. 00 65. 47
	ATOM	2421	0E2	GLU	319	4. 540 -25. 335	86. 913	1. 00 67. 45
	ATOM	2422	C	GLU	319	8. 538 -22. 748	83. 966	1. 00 55. 18
	ATOM	2423	0	GLU	319	9. 278 -22. 324	84. 851	1. 00 55. 23
20	ATOM	2424	N	ALA	320	8. 145 -22. 006	82. 938	1. 00 55. 14
	ATOM	2425	CA	ALA	320	8. 585 -20. 630	82. 780	1. 00 55. 95
	ATOM	2426	CB	ALA	320	8. 609 -20. 265	81. 304	1. 00 55. 13
	ATOM	2427	C	ALA	320	7. 708 -19. 649	83. 544	1. 00 56. 88
	ATOM	2428	0	ALA	320	6. 487 -19. 789	83. 584	1. 00 58. 58
25	ATOM	2429	N	SER	321	8. 344 -18. 648	84. 141	1. 00 57. 00
	ATOM	2430	CA	SER	321	7. 644 -17. 625	84. 902	1. 00 56. 57
	ATOM	2431	CB	SER	321	8. 649 -16. 808	85. 705	1. 00 56. 74
	ATOM	2432	0G	SER	321	8. 013 -15. 725	86. 349	1. 00 57. 41
	ATOM	2433	C	SER	321	6. 853 -16. 689	83. 995	1. 00 58. 61

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	ATOM	2434	0	SER	321	7. 054 -16. 665	82. 783	1. 00 58. 41
	ATOM	2435	N	GLU	322	5. 955 -15. 914	84. 595	1. 00 60. 41
	ATOM	2436	CA	GLU	322	5. 133 -14. 960	83. 858	1. 00 62. 09
	ATOM	2437	CB	GLU	322	4. 171 -14. 254	84. 819	1. 00 65. 34
5	ATOM	2438	CG	GLU	322	3. 185 -13. 299	84. 165	1. 00 69. 70
	ATOM	2439	CD	GLU	322	2. 075 -14. 020	83. 418	1. 00 73. 68
	ATOM	2440	0E1	GLU	322	1. 379 -14. 851	84. 046	1. 00 74. 78
	ATOM	2441	0E2	GLU	322	1. 896 -13. 751	82. 208	1. 00 75. 02
	ATOM	2442	C	GLU	322	6. 047 -13. 929	83. 204	1. 00 61. 24
10	ATOM	2443	0	GLU	322	5. 913 -13. 612	82. 022	1. 00 60. 81
	ATOM	2444	N	GLN	323	6. 987 -13. 420	83. 991	1. 00 60. 42
	ATOM	2445	CA	GLN	323	7. 935 -12. 422	83. 521	1. 00 58. 63
	ATOM	2446	CB	GLN	323	8. 729 -11. 863	84. 700	1. 00 59. 77
	ATOM	2447	CG	GLN	323	7. 902 -11. 039	85. 658	1. 00 61. 20
15	ATOM	2448	CD	GLN	323	8. 690 -10. 608	86. 873	1. 00 63. 03
	ATOM	2449	0E1	GLN	323	9. 672 -9. 866	86. 767	1. 00 63. 70
	ATOM	2450	NE2	GLN	323	8. 266 -11. 074	88. 044	1. 00 64. 05
	ATOM	2451	C	GLN	323	8. 904 -12. 955	82. 478	1. 00 56. 96
	ATOM	2452	0	GLN	323	9. 244 -12. 255	81. 526	1. 00 56. 89
20	ATOM	2453	N	LEU	324	9. 351 -14. 190	82. 652	1. 00 53. 93
	ATOM	2454	CA	LEU	324	10. 298 -14. 763	81. 713	1. 00 52. 62
	ATOM	2455	CB	LEU	324	10. 745 -16. 151	82. 180	1. 00 51. 22
	ATOM	2456	CG	LEU	324	11. 830 -16. 826	81. 334	1. 00 50. 58
	ATOM	2457	CD1	LEU	324	13. 076 -15. 952	81. 299	1. 00 49. 50
25	ATOM	2458	CD2	LEU	324	12. 160 -18. 192	81. 909	1. 00 49. 35
	ATOM	2459	C	LEU	324	9. 730 -14. 855	80. 306	1. 00 52. 38
	ATOM	2460	0	LEU	324	10. 485 -14. 870	79. 337	1. 00 51. 83
	ATOM	2461	N	ARG	325	8. 405 -14. 902	80. 193	1. 00 52. 63
	ATOM	2462	CA	ARG	325	7. 759 -15. 015	78. 887	1. 00 53. 00

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- 101 -ATOM 2463 CB ARG 325 6. 477 -15. 848 79.000 1.00 54.77 ATOM 2464 CG ARG 325 6. 585 -17. 005 79. 985 1. 00 58. 57 ATOM 2465 CDARG 325 6. 013 -18. 330 79.458 1.00 60.34 ATOM 2466 NE ARG 325 6. 881 -18. 961 78.464 1. 00 62. 28 5 ATOM CZ2467 ARG 325 6. 953 -20. 273 78. 249 1. 00 62. 81 ATOM 2468 NH1 ARG 325 6. 208 -21. 109 78. 963 1. 00 62. 98 ATOM 2469 NH2 ARG 325 7. 769 -20. 752 77. 317 1. 00 62. 50 ATOM 2470 C ARG 325 7. 430 -13. 663 78. 266 1. 00 52. 20 **ATOM** 2471 0 ARG 325 6. 835 -13. 595 77. 194 1.00 51.65 ATOM 10 2472 N THR 326 7. 820 -12. 589 78. 940 1. 00 51. 52 ATOM 2473 CA THR 326 7. 562 -11. 248 78. 438 1.00 53.54 ATOM 2474 CB THR 326 7.031 - 10.34379.570 1.00 54.40 **ATOM** 2475 OG1 THR 326 8. 068 -10. 120 80. 534 1. 00 56. 68 **ATOM** 2476 CG2 THR 3265. 858 -11. 012 80. 274 1.00 53.00 15 ATOM 2477 C THR 326 8. 853 -10. 655 77. 850 1.00 54.00 **ATOM** 2478 0 THR 326 9.891 - 10.62678. 515 1.00 53.48 **ATOM** 2479 N ARG 3278. 782 -10. 191 76.604 1.00 54.30 ATOM 2480 CA ARG 327 9. 948 -9. 628 75. 923 1. 00 55. 25 ATOM 2481 CB ARG 327 9.568 - 9.07474. 550 1. 00 58. 73 ATOM 20 2482 CG ARG 327 9.050 - 10.10173. 572 1.00 62.94 ATOM 2483 CD ARG 327 9. 189 -9. 599 72. 143 1.00 66.63 **ATOM** 2484 NE ARG 3278. 462 -10. 454 71. 213 1. 00 70. 25 ATOM 2485 CZARG 3277. 136 -10. 522 71. 154 1. 00 72. 29 ATOM 2486 NH1 ARG 327 6. 399 -9. 778 71. 969 1.00 72.86 ATOM 25 2487 NH2 ARG 327 6.546 - 11.33870. 288 1.00 73.24 ATOM 2488 C ARG 327 10. 660 -8. 529 76. 688 1. 00 53. 79 ATOM 2489 0 ARG 32710. 027 -7.69077. 326 1. 00 55. 10 ATOM 2490 N GLY 328 11. 986 -8. 535 76.604 1.00 50.97 ATOM

2491

CA

GLY

328

12. 773

-7.520

77. 276

1. 00 50. 03

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	ATOM	2492	C	GLY	328	12. 922	-7. 715	78. 770	1. 00 49. 36
	ATOM	2493	0	GLY	328	13. 622	-6. 942	79. 426	1. 00 49. 68
	ATOM	2494	N	ALA	329	12. 274	-8. 740	79. 315	1. 00 47. 47
	ATOM	2495	CA	ALA	329	12. 354	-9. 007	80. 749	1. 00 46. 93
5	ATOM	2496	CB	ALA	329	11. 468	-10. 184	81. 115	1. 00 48. 23
	ATOM	2497	C	ALA	329	13. 786	-9. 287	81. 173	1. 00 45. 48
	ATOM	2498	0	ALA	329	14. 247	-8. 794	82. 203	1. 00 44. 91
	ATOM	2499	N	PHE	330	14. 490	-10. 088	80. 383	1. 00 43. 75
	ATOM	2500	CA	PHE	330	15. 870	-10. 392	80. 710	1. 00 42. 95
10	ATOM	2501	CB	PHE	330	16. 271	-11. 760	80. 156	1. 00 39. 40
	ATOM	2502	CG	PHE	330	17. 478	-12. 350	80. 829	1. 00 36. 90
	ATOM	2503	CD1	PHE	330	18. 761	-11. 985	80. 436	1. 00 35. 73
	ATOM	2504	CD2	PHE	330	17. 330	-13. 241	81. 893	1. 00 35. 23
	ATOM	2505	CE1	PHE	330	19. 878	-12. 496	81. 093	1. 00 33. 48
15	ATOM	2506	CE2	PHE	330	18. 443	-13. 759	82. 558	1. 00 31. 61
	ATOM	2507	CZ	PHE	330	19. 716	-13. 387	82. 160	1. 00 33. 39
	ATOM	2508	C	PHE	330	16. 752	-9. 292	80. 130	1. 00 43. 51
	ATOM	2509	0	PHE	330	17. 202	-9. 373	78. 986	1. 00 44. 11
	ATOM	2510	N	GLU	331	16. 962	-8. 254	80. 935	1. 00 43. 95
20	ATOM	2511	CA	GLU	331	17. 777	-7. 099	80. 569	1. 00 43. 11
	ATOM	2512	CB	GLU	331	17. 767	-6. 068	81. 697	1. 00 46. 19
	ATOM	2513	CG	GLU	331	16. 393	-5. 551	82. 092	1. 00 50. 13
	ATOM	2514	CD	GLU	331	16. 458	-4. 651	83. 316	1. 00 53. 54
	ATOM	2515	0E1	GLU	331	17. 324	-3. 745	83. 343	1. 00 55. 03
25	ATOM	2516	OE2	GLU	331	15. 646	-4. 846	84. 247	1. 00 53. 56
	ATOM	2517	C	GLU	331	19. 216	-7. 511	80. 310	1. 00 42. 02
	ATOM	2518	0	GLU	331	19. 742	-8. 411	80. 968	1. 00 42. 05
	ATOM	2519	N	THR	332	19. 855	-6. 830	79. 365	1. 00 39. 23
	ATOM	2520	CA	THR	332	21. 235	-7. 122	79. 017	1. 00 36. 08

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	ATOM	2521	CB	THR	332	21. 713	-6. 200	77. 869	1. 00 36. 47
	ATOM	2522	0G	1 THR	332	21. 297	-6. 762	76. 618	1. 00 33. 61
	ATOM	2523	CG	2 THR	332	23. 235	-6. 030	77. 884	1. 00 31. 36
	ATOM	2524	C	THR	332	22. 159	-6. 987	80. 219	1. 00 35. 73
5	ATOM	2525	0	THR	332	23. 209	-7. 634	80. 280	1. 00 35. 30
	ATOM	2526	N	ARG	333	21. 782	-6. 151	81. 180	1. 00 34. 21
	ATOM	2527	CA	ARG	333	22. 632	-6. 003	82. 353	1. 00 34. 18
	ATOM	2528	CB	ARG	333	22. 211	-4. 786	83. 193	1. 00 36. 60
	ATOM	2529	CG	ARG	333	20. 830	-4. 854	83. 835	1. 00 39. 58
10	ATOM	2530	CD	ARG	333	20. 488	-3. 518	84. 520	1. 00 42. 78
	ATOM	2531	NE	ARG	333	19. 264	-3. 590	85. 316	1. 00 45. 29
	ATOM	2532	CZ	ARG	333	19. 205	-4. 039	86. 567	1. 00 47. 32
	ATOM	2533	NH1	ARG	333	20. 305	-4. 455	87. 182	1. 00 49. 55
	ATOM	2534	NH2	ARG	333	18. 042	-4. 080	87. 205	1. 00 48. 70
15	ATOM	2535	C	ARG	333	22. 609	-7. 298	83. 181	1. 00 31. 65
	ATOM	2536	0	ARG	333	23. 584	-7. 625	83. 863	1. 00 31. 61
	ATOM	2537	N	PHE	334	21. 513	-8. 049	83. 105	1. 00 31. 01
	ATOM	2538	CA	PHE	334	21. 431	-9. 317	83. 835	1. 00 30. 67
	ATOM	2539	CB	PHE	334	20. 048	-9. 967	83. 678	1. 00 30. 39
20	ATOM	2540	CG	PHE	334	18. 923	-9. 210	84. 330	1. 00 30. 58
	ATOM	2541	CD1	PHE	334	19. 170	-8. 214	85. 269	1. 00 29. 37
	ATOM	2542	CD2	PHE	334	17. 600	-9. 522	84. 019	1. 00 31. 94
	ATOM	2543		PHE	334	18. 113	-7. 539	85. 891	1. 00 31. 67
	ATOM	2544	CE2	PHE	334	16. 535	-8. 851	84. 636	1. 00 32. 25
25	ATOM	2545	CZ	PHE	334	16. 796	-7. 857	85. 575	1. 00 28. 89
	ATOM	2546	C	PHE	334	22. 496 -	-10. 287	83. 295	1. 00 30. 73
	ATOM	2547	0	PHE	334	23. 136 -	11. 016	84. 064	1. 00 30. 77
	ATOM	2548	N	VAL	335	22. 685 -	10. 290	81. 973	1. 00 29. 44
	ATOM	2549	CA	VAL	335	23. 672 -	11. 165	81. 350	1. 00 30. 61

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	ATOM	2550	CB	VAL	335	23. 777 -10. 921	79. 831	1. 00 30. 75
	ATOM	2551	CG1	VAL	335	24. 774 -11. 898	79. 216	1. 00 32. 48
	ATOM	2552	CG2	VAL	335	22. 424 -11. 078	79. 181	1. 00 29. 80
	ATOM	2553	C	VAL	335	25. 041 -10. 904	81. 964	1. 00 31. 64
5	ATOM	2554	0	VAL	335	25. 759 -11. 830	82. 356	1. 00 31. 87
	ATOM	2555	N	SER	336	25. 382 -9. 623	82. 048	1. 00 33. 23
	ATOM	2556	CA	SER	336	26. 655 -9. 173	82. 593	1. 00 32. 42
	ATOM	2557	CB	SER	336	26. 778 -7. 660	82. 384	1. 00 33. 94
	ATOM	2558	0G	SER	336	28. 080 -7. 204	82. 682	1. 00 38. 27
10	ATOM	2559	C	SER	336	26. 793 -9. 524	84. 078	1. 00 32. 82
	ATOM	2560	0	SER	336	27. 863 -9. 917	84. 529	1. 00 33. 76
	ATOM	2561	N	GLN	337	25. 711 -9. 389	84. 839	1. 00 32. 64
	ATOM	2562	CA	GLN	337	25. 753 -9. 715	86. 260	1. 00 34. 83
	ATOM	2563	CB	GLN	337	24. 480 -9. 233	86. 958	1. 00 37. 43
15	ATOM	2564	CG	GLN	337	24. 339 -7. 721	86. 972	1. 00 42. 29
	ATOM	2565	CD	GLN	337	22. 984 -7. 260	87. 471	1. 00 44. 59
	ATOM	2566	0E1	GLN	337	22. 710 -6. 062	87. 525	1. 00 46. 49
	ATOM	2567	NE2	GLN	337	22. 128 -8. 209	87. 835	1. 00 43. 79
	ATOM	2568	C	GLN	337	25. 899 -11. 217	86. 447	1. 00 33. 66
20	ATOM	2569	0	GLN	337	26. 663 -11. 674	87. 297	1. 00 35. 28
	ATOM	2570	N	VAL	338	25. 159 -11. 983	85. 655	1. 00 31. 29
	ATOM	2571	CA	VAL	338	25. 236 -13. 432	85. 743	1. 00 29. 21
	ATOM	2572	CB	VAL	338	24. 326 -14. 102	84. 690	1. 00 28. 27
	ATOM	2573	CG1	VAL	338	24. 687 -15. 571	84. 525	1. 00 27. 17
25	ATOM	2574	CG2	VAL	338	22. 877 -13. 984	85. 129	1. 00 26. 99
	ATOM	2575	C	VAL	338	26. 678 -13. 877	85. 547	1. 00 27. 35
	ATOM	2576	0	VAL	338	27. 176 -14. 722	86. 284	1. 00 26. 69
	ATOM	2577	N	GLU	339	27. 361 -13. 283	84. 576	1. 00 27. 29
	ATOM	2578	CA	GLU	339	28. 747 -13. 657	84. 314	1. 00 27. 15

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	ATOM	2579	CB	GLU	339	29. 136 -13. 303	82. 871	1. 00 27. 02
	ATOM	2580	CG	GLU	339	28. 404 -14. 185	81. 843	1. 00 30. 73
	ATOM	2581	CD	GLU	339	28. 942 -14. 063	80. 425	1. 00 30. 33
	ATOM	2582	0E1	GLU	339	30. 121 -14. 414	80. 185	1. 00 34. 73
5	ATOM	2583	0E2	GLU	339	28. 179 -13. 619	79. 548	1. 00 29. 50
	ATOM	2584	C	GLU	339	29. 749 -13. 085	85. 311	1. 00 26. 93
	ATOM	2585	0	GLU	339	30. 940 -13. 345	85. 209	1. 00 27. 69
	ATOM	2586	N	SER	340	29. 264 -12. 320	86. 285	1. 00 27. 55
	ATOM	2587	CA	SER	340	30. 140 -11. 763	87. 318	1. 00 28. 61
10	ATOM	2588	CB	SER	340	29. 741 -10. 323	87. 667	1. 00 29. 40
	ATOM	2589	0G	SER	340	29. 800 -9. 485	86. 528	1. 00 35. 97
	ATOM	2590	C	SER	340	30. 029 -12. 615	88. 583	1. 00 27. 94
	ATOM	2591	0	SER	340	30. 811 -12. 448	89. 526	1. 00 24. 04
	ATOM	2592	N	ASP	341	29. 042 -13. 511	88. 600	1. 00 28. 02
15	ATOM	2593	CA	ASP	341	28. 812 -14. 387	89. 748	1. 00 29. 66
	ATOM	2594	CB	ASP	341	27. 808 -15. 490	89. 393	1. 00 30. 94
	ATOM	2595	CG	ASP	341	27. 296 -16. 227	90. 620	1. 00 33. 11
	ATOM	2596	OD 1	ASP	341	26. 289 -15. 778	91. 217	1. 00 28. 78
	ATOM	2597	OD2	ASP	341	27. 918 -17. 247	90. 991	1. 00 32. 82
20	ATOM	2598	C	ASP	341	30. 137 -15. 003	90. 163	1. 00 30. 38
	ATOM	2599	0	ASP	341	30. 853 -15. 564	89. 342	1. 00 30. 59
	ATOM	2600	N	THR	342	30. 466 -14. 886	91. 443	1. 00 33. 59
	ATOM	2601	CA	THR	342	31. 729 -15. 405	91. 953	1. 00 37. 01
	ATOM	2602	CB	THR	342	32. 013 -14. 836	93. 350	1. 00 38. 81
25	ATOM	2603	0G1	THR	342	31. 012 -15. 304	94. 265	1. 00 43. 90
	ATOM	2604	CG2	THR	342	31. 972 -13. 316	93. 317	1. 00 35. 79
	ATOM	2605	C	THR	342	31. 780 -16. 929	92. 027	1. 00 37. 87
	ATOM	2606	0	THR	342	32. 853 -17. 514	92. 191	1. 00 39. 64
	MOTA	2607	N	GLY	343	30. 625 -17. 568	91. 894	1. 00 36. 81

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	ATOM	2608	CA	GLY	343	30. 578 -19. 018	91. 970	1. 00 39. 26
	ATOM	2609	C	GLY	343	29. 631 -19. 515	93. 053	1. 00 38. 98
	ATOM	2610	0	GLY	. 343	29. 293 -20. 695	93. 090	1. 00 39. 46
	ATOM	2611	N	ASP	344	29. 204 -18. 615	93. 935	1. 00 38. 20
5	ATOM	2612	CA	ASP	344	28. 287 -18. 980	95. 005	1. 00 39. 74
	ATOM	2613	CB	ASP	344	28. 480 -18. 071	96. 231	1. 00 39. 14
	ATOM	2614	CG	ASP	344	28. 267 -16. 595	95. 928	1. 00 41. 19
	ATOM	2615	OD1	ASP	344	27. 733 -16. 256	94. 848	1. 00 39. 57
	ATOM	2616	0D2	ASP	344	28. 627 -15. 767	96. 794	1. 00 42. 27
10	ATOM	2617	C	ASP	344	26. 842 -18. 926	94. 516	1. 00 40. 25
	ATOM	2618	0	ASP	344	25. 904 -19. 235	95. 257	1. 00 39. 36
	ATOM	2619	N	ARG	345	26. 680 -18. 525	93. 259	1. 00 38. 45
	ATOM	2620	CA	ARG	345	25. 374 -18. 449	92. 618	1. 00 37. 30
	ATOM	2621	CB	ARG	345	24. 738 -19. 847	92. 587	1. 00 37. 49
15	ATOM	2622	CG	ARG	345	25. 657 -20. 935	92. 044	1. 00 38. 81
	ATOM	2623	CD	ARG	345	24. 976 -22. 301	92. 046	1. 00 40. 19
	ATOM	2624	NE	ARG	345	25. 790 -23. 327	91. 397	1. 00 42. 18
	ATOM	2625	CZ	ARG	345	26. 730 -24. 051	91. 999	1. 00 43. 19
	ATOM	2626	NH1	ARG	345	26. 990 -23. 880	93. 288	1. 00 43. 31
20	ATOM	2627	NH2	ARG	345	27. 421 -24. 947	91. 302	1. 00 40. 56
	ATOM	2628	C	ARG	345	24. 397 -17. 456	93. 246	1. 00 37. 06
	ATOM	2629	0	ARG	345	23. 231 -17. 395	92. 837	1. 00 35. 44
	ATOM	2630	N	LYS	346	24. 855 -16. 681	94. 228	1. 00 37. 09
	ATOM	2631	CA	LYS	346	23. 977 -15. 704	94. 876	1. 00 39. 61
25	ATOM	2632	CB	LYS	346	24. 710 -14. 964	96. 005	1. 00 43. 18
	ATOM	2633	CG	LYS	346	25. 084 -15. 826	97. 214	1. 00 47. 92
	ATOM	2634	CD	LYS	346	25. 835 -15. 009	98. 285	1. 00 50. 48
	ATOM	2635	CE	LYS	346	26. 274 -15. 887	99. 466	1. 00 53. 20
	ATOM	2636	NZ	LYS	346	27. 039 -15. 136	100. 520	1. 00 54. 15

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	ATOM	2637	C	LYS	346	23. 467 -14. 690	93. 858	1. 00 39. 25
	ATOM	2638	0	LYS	346	22. 271 -14. 400	93. 795	1. 00 38. 51
	ATOM	2639	N	GLN	347	24. 384 -14. 158	93. 055	1. 00 40. 01
	ATOM	2640	CA	GLN	347	24. 036 -13. 169	92. 037	1. 00 39. 62
5	ATOM	2641	CB	GLN	347	25. 301 -12. 725	91. 290	1. 00 44. 30
	MOTA	2642	CG	GLN	347	25. 117 -11. 507	90. 403	1. 00 50. 12
	MOTA	2643	CD	GLN	347	24. 996 -10. 214	91. 196	1. 00 54. 40
	ATOM	2644	0E1	GLN	347	24. 699 -9. 153	90. 637	1. 00 57. 36
	ATOM	2645	NE2	GLN	347	25. 234 -10. 295	92. 501	1. 00 55. 02
10	ATOM	2646	C	GLN	347	23. 015 -13. 735	91. 046	1. 00 36. 71
	ATOM	2647	0	GLN	347	22. 012 -13. 087	90. 732	1. 00 35. 38
	ATOM	2648	N	ILE	348	23. 264 -14. 949	90. 563	1. 00 33. 61
	ATOM	2649	CA	ILE	348	22. 360 -15. 579	89. 610	1. 00 30. 26
	ATOM	2650	CB	ILE	348	22. 946 -16. 906	89. 103	1. 00 31. 09
15	ATOM	2651	CG2	ILE	348	21. 983 -17. 561	88. 102	1. 00 24. 14
	ATOM	2652	CG1	ILE	348	24. 315 -16. 641	88. 467	1. 00 24. 89
	ATOM	2653	CD1	ILE	348	25. 016 -17. 870	87. 989	1. 00 26. 20
	ATOM	2654	C	ILE	348	20. 990 -15. 836	90. 231	1. 00 32. 47
	ATOM	2655	0	ILE	348	19. 946 -15. 578	89. 607	1. 00 28. 48
20	ATOM	2656	N	TYR	349	20. 996 -16. 330	91. 468	1. 00 33. 64
	ATOM	2657	CA	TYR	349	19. 757 -16. 622	92. 173	1. 00 33. 94
	ATOM	2658	CB	TYR	349	20. 023 -17. 189	93. 566	1. 00 35. 19
	ATOM	2659	CG	TYR	349	18. 728 -17. 513	94. 273	1. 00 35. 54
	ATOM	2660	CD1	TYR	349	18. 085 -18. 737	94. 064	1. 00 35. 44
25	ATOM	2661	CE1	TYR	349	16. 847 -19. 009	94. 647	1. 00 35. 96
	ATOM	2662	CD2	TYR	349	18. 100 -16. 569	95. 083	1. 00 34. 28
	ATOM	2663	CE2	TYR	349	16. 860 -16. 833	95. 665	1. 00 34. 50
	ATOM	2664	CZ	TYR	349	16. 242 -18. 053	95. 441	1. 00 34. 82
	MOTA	2665	ОН	TYR	349	15. 007 -18. 305	95. 990	1. 00 39. 44

- 108 -ATOM 2666 C TYR 18. 888 -15. 390 92. 339 1. 00 35. 45 349 **ATOM** 2667 0 TYR 349 17. 698 -15. 419 92.042 1. 00 37. 11 ATOM 2668 N ASN 350 19. 475 -14. 312 92. 846 1. 00 37. 18 ATOM 2669 ASN 350 18. 722 -13. 082 93.049 1. 00 38. 47 CA CB 5 ATOM 2670 ASN 350 19. 617 -11. 985 93. 630 1. 00 40. 65 ATOM CG 20. 014 -12. 263 95.065 2671 ASN 350 1. 00 45. 75 ATOM 2672 OD1 ASN 350 19. 176 -12. 638 95.893 1. 00 45. 11 ND2 ASN ATOM 2673 350 21. 298 -12. 075 95. 373 1. 00 46. 81 ATOM 2674 C ASN 350 18. 085 -12. 585 91. 768 1. 00 37. 56 ATOM 2675 0 ASN 350 16. 924 -12. 186 91. 769 1. 00 40. 92 10 ATOM 2676 N ILE 351 18. 839 -12. 601 90.673 1. 00 37. 62 1. 00 37. 09 ATOM 2677CA ILE 351 18. 310 -12. 139 89. 395 ATOM 2678 CB ILE 351 19. 401 -12. 130 88. 308 1. 00 38. 11 ATOM CG2 ILE 86. 938 2679 351 18. 771 -11. 955 1. 00 37. 56 15 ATOM 2680 CG1 ILE 351 20. 400 -11. 004 88. 588 1. 00 38. 11 ATOM CD1 ILE 2681 351 21. 726 -11. 178 87. 879 1. 00 36. 24 2682 C ATOM ILE 351 17. 144 -12. 997 88. 921 1. 00 36. 57 16. 120 -12. 474 88. 479 ATOM 2683 0 ILE 351 1. 00 38. 22 ATOM 2684 N LEU 17. 291 -14. 314 89. 012 352 1. 00 35. 96 **ATOM** 2685 CA 88. 577 20 LEU 352 16. 219 -15. 206 1. 00 36. 28 **ATOM** 2686 CB LEU 352 16. 740 -16. 640 88. 443 1. 00 32. 41 CG ATOM 2687 LEU 352 17. 845 -16. 828 87. 395 1. 00 30. 66 ATOM 2688 CD1 LEU 18. 465 -18. 226 87. 496 352 1. 00 25. 83 CD2 LEU 86. 025 ATOM 2689 352 17. 262 -16. 597 1. 00 27. 66 15. 039 -15. 156 25 ATOM 2690 C LEU 352 89. 547 1. 00 37. 27 ATOM 2691 0 LEU 352 13. 896 -15. 356 89. 145 1. 00 38. 32 2692 15. 322 -14. 888 90. 819 ATOM N SER 353 1. 00 39. 41

ATOM

ATOM

2693

2694

CA

CB

SER

SER

353

353

14. 279 -14. 794 91. 838

14. 893 -14. 708 93. 237

1. 00 42. 13

1. 00 43. 72

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	ATOM	2695	0G	SER	353	13. 883 -14. 546	94. 224	1. 00 48. 17
	ATOM	2696	C	SER	353	13. 431 -13. 557	91. 590	1. 00 43. 61
	ATOM	2697	0	SER	353	12. 229 -13. 552	91. 858	1. 00 42. 99
	ATOM	2698	N	THR	354	14. 066 -12. 506	91. 081	1. 00 44. 80
5	ATOM	2699	CA	THR	354	13. 363 -11. 267	90. 785	1. 00 46. 06
	ATOM	2700	CB	THR	354	14. 356 -10. 122	90. 497	1. 00 47. 48
	ATOM	2701	0G1	THR	354	15. 100 -9. 820	91. 687	1. 00 47. 39
	ATOM	2702	CG2	THR	354	13. 615 -8. 877	90. 034	1. 00 47. 87
	MOTA	2703	C	THR	354	12. 446 -11. 455	89. 579	1. 00 46. 06
10	MOTA	2704	0	THR	354	11. 443 -10. 757	89. 436	1. 00 47. 23
	MOTA	2705	N	LEU	355	12. 788 -12. 406	88. 717	1. 00 46. 03
	ATOM	2706	CA	LEU	355	11. 983 -12. 679	87. 533	1. 00 46. 26
	ATOM	2707	CB	LEU	355	12. 875 -13. 157	86. 390	1. 00 46. 43
	ATOM	2708	CG	LEU	355	14. 030 -12. 210	86. 063	1. 00 46. 85
15	ATOM	2709	CD1	LEU	355	14. 861 -12. 813	84. 950	1. 00 47. 00
	ATOM	2710	CD2	LEU	355	13. 497 -10. 844	85. 660	1. 00 45. 99
	ATOM	2711	C	LEU	355	10. 908 -13. 722	87. 821	1. 00 46. 88
	ATOM	2712	0	LEU	355	10. 370 -14. 346	86. 902	1. 00 47. 28
	ATOM	2713	N	GLY	356	10. 609 -13. 912	89. 105	1. 00 47. 29
20	ATOM	2714	CA	GLY	356	9. 586 -14. 858	89. 511	1. 00 44. 74
	ATOM	2715	C	GLY	356	9. 959 -16. 321	89. 396	1. 00 44. 45
	ATOM	2716	0	GLY	356	9. 097 -17. 163	89. 146	1. 00 45. 09
	ATOM	2717	N	LEU	357	11. 235 -16. 635	89. 575	1. 00 43. 26
	ATOM	2718	CA	LEU	357	11. 681 -18. 018	89. 485	1. 00 41. 29
25	ATOM	2719	CB	LEU	357	12. 653 -18. 187	88. 310	1. 00 42. 15
	ATOM	2720	CG	LEU	357	12. 171 -17. 833	86. 896	1. 00 41. 21
	ATOM	2721	CD1	LEU	357	13. 366 -17. 781	85. 972	1. 00 39. 61
	ATOM	2722	CD2	LEU	357	11. 153 -18. 849	86. 393	1. 00 39. 50
	ATOM	2723	C	LEU	357	12. 361 -18. 455	90. 780	1. 00 40. 57

- 110 -**ATOM** 2724 0 LEU 357 12. 780 -17. 627 91. 590 1. 00 38. 53 90. 970 **ATOM** 2725 N ARG 358 12. 448 -19. 766 1. 00 39. 68 ATOM 2726 ARG 13. 092 -20. 355 92. 139 1.00 40.04 CA 358 ATOM 2727 CB ARG 358 12.048 - 20.91693. 112 1. 00 42. 61 ATOM 2728 CG ARG 11. 172 -19. 845 93. 760 358 1. 00 46. 08 5 ATOM 2729 CDARG 358 12. 019 -18. 871 94. 560 1. 00 49. 74 **ATOM** 2730 NE ARG 358 11. 355 -17. 588 94. 772 1. 00 55. 41 CZATOM 2731 ARG 358 10. 588 -17. 293 95. 816 1. 00 58. 08 NH1 ARG 10. 376 -18. 195 ATOM 2732 358 96. 771 1. 00 59. 09 ATOM 2733 NH2 ARG 95. 906 358 10. 035 -16. 087 1. 00 58. 98 10 2734 C **ATOM** ARG 358 13. 954 -21. 471 91. 576 1. 00 38. 39 ATOM 2735 0 ARG 358 13. 569 -22. 641 91. 586 1. 00 37. 47 **ATOM** 2736 N PR₀ 15. 140 -21. 109 91. 065 359 1. 00 36. 51 2737 PR0 15. 664 -19. 728 91. 087 **ATOM** CD 359 1. 00 36. 88 ATOM 2738 CA PR0 359 16. 123 -22. 006 90. 461 1. 00 34. 17 15 ATOM 2739 CBPR0 17. 035 -21. 039 89. 722 359 1. 00 35. 29 2740 CG 17. 135 -19. 925 90. 703 ATOM PR0 359 1. 00 34. 03 ATOM 2741 C PR0 359 16. 915 -22. 872 91. 416 1. 00 33. 10 2742 ATOM 0 PR0 359 17. 140 -22. 520 92. 566 1. 00 31. 20 ATOM 2743 N SER 360 17. 365 -24. 004 90. 899 1. 00 33. 97 20 ATOM 2744 CA SER 360 18. 183 -24. 931 91. 658 1. 00 34. 21 ATOM 2745 CB SER 360 17. 912 -26. 363 91. 210 1. 00 34. 53 2746 0G SER 18. 287 -26. 530 89. 851 1.00 33.54 ATOM 360 ATOM 2747 C SER 360 19. 618 -24. 568 91. 307 1.00 34.99 ATOM 2748 0 SER 360 19. 855 -23. 673 90. 495 1. 00 35. 49 25 ATOM 2749N THR 361 20. 564 -25. 267 91. 920 1.00 34.70 2750 21. 977 -25. 048 ATOM CA THR 361 91. 673 1. 00 36. 89 ATOM 2751 CB THR 361 22. 838 -26. 003 92. 535 1. 00 36. 99

2752

ATOM

OG1 THR

361

22. 828 -25. 558 93. 898

1. 00 38. 93

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	ATOM	2753	CG2	THR	361	24. 260 -26. 041	92. 033	1. 00 38. 24
	ATOM	2754	C	THR	361	22. 303 -25. 291	90. 201	1. 00 37. 14
	ATOM	2755	0	THR	361	23. 142 -24. 606 ⁻	89. 616	1. 00 37. 81
	ATOM	2756	N	THR	362	21. 635 -26. 273	89. 612	1. 00 35. 92
5	ATOM	2757	CA	THR	362	21. 865 -26. 614	88. 223	1. 00 34. 91
	ATOM	2758	CB	THR	362	21. 369 -28. 037	87. 914	1. 00 36. 12
	ATOM	2759	0G1	THR	362	19. 969 -28. 117	88. 199	1. 00 40. 45
	ATOM	2760	CG2	THR	362	22. 113 -29. 063	88. 771	1. 00 34. 62
	ATOM	2761	C	THR	362	21. 181 -25. 626	87. 292	1. 00 33. 53
10	ATOM	2762	0	THR	362	21. 684 -25. 360	86. 205	1. 00 33. 46
	ATOM	2763	N	ASP	363	20. 034 -25. 091	87. 698	1. 00 31. 06
	ATOM	2764	CA	ASP	363	19. 355 -24. 115	86. 860	1. 00 32. 46
	ATOM	2765	CB	ASP	363	18. 018 -23. 690	87. 468	1. 00 34. 45
	ATOM	2766	CG	ASP	363	16. 964 -24. 783	87. 409	1. 00 37. 91
15	ATOM	2767	OD1	ASP	363	16. 889 -25. 504	86. 388	1. 00 38. 99
	ATOM	2768	OD2	ASP	363	16. 194 -24. 907	88. 385	1. 00 38. 23
	ATOM	2769	C	ASP	363	20. 254 -22. 878	86. 718	1. 00 32. 88
	ATOM	2770	0	ASP	363	20. 419 -22. 331	85. 629	1. 00 30. 65
	ATOM	2771	N	CYS	364	20. 833 -22. 451	87. 836	1. 00 33. 86
20	ATOM	2772	CA	CYS	364	21. 712 -21. 292	87. 860	1. 00 32. 22
	ATOM	2773	CB	CYS	364	22. 186 -21. 015	89. 289	1. 00 31. 35
	ATOM	2774	SG	CYS	364	20. 915 -20. 338	90. 389	1. 00 31. 77
	ATOM	2775	C	CYS	364	22. 914 -21. 493	86. 950	1. 00 30. 91
	ATOM	2776	0	CYS	364	23. 207 -20. 645	86. 119	1. 00 30. 71
25	ATOM	2777	N	ASP	365	23. 608 -22. 614	87. 107	1. 00 31. 25
	ATOM	2778	CA	ASP	365	24. 774 -22. 894	86. 280	1. 00 32. 00
	ATOM	2779	СВ	ASP	365	25. 389 -24. 243	86. 659	1. 00 32. 78
	ATOM	2780	CG	ASP	365	26. 037 -24. 211	88. 023	1. 00 35. 48
	ATOM	2781	0D1	ASP	365	26. 017 -23. 127	88. 650	1. 00 37. 01

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	ATOM	2782	OD2	ASP	365	26. 564 -25. 251	88. 466	1. 00 35. 21
	ATOM	2783	C	ASP	365	24. 405 -22. 886	84. 810	1. 00 30. 41
	ATOM	2784	0	ASP	365	25. 166 -22. 407	83. 966	1. 00 31. 73
	ATOM	2785	N	ILE	366	23. 225 -23. 408	84. 514	1. 00 29. 17
5	ATOM	2786	CA	ILE	366	22. 739 -23. 462	83. 148	1. 00 30. 58
	ATOM	2787	CB	ILE	366	21. 456 -24. 318	83. 058	1. 00 30. 61
	ATOM	2788	CG2	ILE	366	20. 779 -24. 118	81. 712	1. 00 28. 15
	ATOM	2789	CG1	ILE	366	21. 808 -25. 797	83. 261	1. 00 33. 09
	ATOM	2790	CD1	ILE	366	20. 577 -26. 702	83. 405	1. 00 32. 69
10	ATOM	2791	C	ILE	366	22. 462 -22. 066	82. 576	1. 00 29. 08
	ATOM	2792	0	ILE	366	22. 729 -21. 815	81. 405	1. 00 28. 78
	ATOM	2793	N	VAL	367	21. 906 -21. 170	83. 386	1. 00 27. 52
	ATOM	2794	CA	VAL	367	21. 632 -19. 817	82. 910	1. 00 27. 71
	ATOM	2795	CB	VAL	367	20. 803 -19. 021	83. 943	1. 00 26. 66
15	ATOM	2796	CG1	VAL	367	20. 812 -17. 531	83. 609	1. 00 24. 57
	ATOM	2797	CG2	VAL	367	19. 373 -19. 535	83. 928	1. 00 26. 09
	ATOM	2798	C	VAL	367	22. 979 -19. 143	82. 643	1. 00 28. 05
	ATOM	2799	0	VAL	367	23. 144 -18. 409	81. 670	1. 00 28. 53
	ATOM	2800	N	ARG	368	23. 940 -19. 436	83. 508	1. 00 27. 74
20	ATOM	2801	CA	ARG	368	25. 300 -18. 927	83. 386	1. 00 30. 76
	ATOM	2802	CB	ARG	368	26. 172 -19. 575	84. 458	1. 00 31. 66
	ATOM	2803	CG	ARG	368	27. 023 -18. 648	85. 269	1. 00 38. 26
	ATOM	2804	CD	ARG	368	28. 312 -18. 282	84. 579	1. 00 41. 00
	ATOM	2805	NE	ARG	368	29. 272 -17. 763	85. 547	1. 00 43. 72
25	ATOM	2806	CZ	ARG	368	30. 397 -17. 135	85. 226	1. 00 46. 75
	ATOM	2807	NH1	ARG	368	30. 710 -16. 938	83. 954	1. 00 48. 06
	ATOM	2808	NH2	ARG	368	31. 212 -16. 708	86. 179	1. 00 47. 96
	ATOM	2809	C	ARG	368	25. 841 -19. 317	82. 003	1. 00 30. 63
	ATOM	2810	0	ARG	368	26. 343 -18. 469	81. 256	1. 00 27. 84

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	ATOM	2811	N	ARG	369	25. 735 -20. 606	81. 677	1. 00 27. 70
	ATOM	2812	CA	ARG	369	26. 228 -21. 115	80. 399	1. 00 28. 24
	ATOM	2813	CB	ARG	369	26. 077 -22. 645	80. 327	1. 00 26. 69
	ATOM	2814	CG	ARG	369	27. 044 -23. 429	81. 224	1. 00 29. 04
5	MOTA	2815	CD	ARG	369	28. 506 -23. 228	80. 815	1. 00 31. 91
	ATOM	2816	NE	ARG	369	28. 752 -23. 683	79. 445	1. 00 35. 74
	MOTA	2817	CZ	ARG	369	29. 117 -22. 892	78. 439	1. 00 36. 75
	ATOM	2818	NH1	ARG	369	29. 291 -21. 590	78. 638	1. 00 36. 65
	ATOM	2819	NH2	ARG	369	29. 291 -23. 400	77. 225	1. 00 36. 11
10	ATOM	2820	C	ARG	369	25. 528 -20. 472	79. 208	1. 00 27. 14
	ATOM	2821	0	ARG	369	26. 160 -20. 188	78. 189	1. 00 28. 06
	ATOM	2822	N	ALA	370	24. 224 -20. 252	79. 327	1. 00 25. 64
	ATOM	2823	CA	ALA	370	23. 480 -19. 634	78. 238	1. 00 25. 08
	ATOM	2824	CB	ALA	370	21. 991 -19. 587	78. 574	1. 00 25. 47
15	ATOM	2825	C	ALA	370	24. 015 -18. 218	78. 006	1. 00 25. 14
	ATOM	2826	0	ALA	370	24. 196 -17. 793	76. 870	1. 00 25. 23
	ATOM	2827	N	CYS	371	24. 268 -17. 491	79. 087	1. 00 24. 15
	ATOM	2828	CA	CYS	371	24. 785 -16. 135	78. 965	1. 00 25. 09
	ATOM	2829	CB	CYS	371	24. 855 -15. 467	80. 338	1. 00 22. 74
20	ATOM	2830	SG	CYS	371	23. 239 -15. 076	81. 033	1. 00 25. 40
	ATOM	2831	C	CYS	371	26. 161 -16. 127	78. 300	1. 00 24. 93
	ATOM	2832	0	CYS	371	26. 392 -15. 358	77. 367	1. 00 25. 49
	ATOM	2833	N	GLU	372	27. 062 -16. 991	78. 765	1. 00 24. 70
	ATOM	2834	CA	GLU	372	28. 411 -17. 073	78. 207	1. 00 26. 69
25	ATOM	2835	CB	GLU	372	29. 247 -18. 105	78. 975	1. 00 27. 07
	ATOM	2836	CG	GLU	372	29. 232 -17. 890	80. 481	1. 00 32. 77
	ATOM	2837	CD	GLU	372	30. 016 -18. 945	81. 243	1. 00 33. 87
	ATOM	2838	0E1	GLU	372	29. 905 -20. 139	80. 892	1. 00 36. 95
	ATOM	2839	0E2	GLU	372	30. 733 -18. 583	82. 200	1. 00 35. 18

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	ATOM	2840	C	GLU	372	28. 418 -17. 420	76. 718	1. 00 27. 23
	ATOM	2841	0	GLU	372	29. 259 -16. 922	75. 966	1. 00 29. 09
	ATOM	2842	N	SER	373	27. 489 -18. 273	76. 296	1. 00 25. 93
	ATOM	2843	CA	SER	373	27. 403 -18. 664	74. 894	1. 00 27. 07
5	ATOM	2844	CB	SER	373	26. 393 -19. 803	74. 718	1. 00 25. 93
	ATOM	2845	0G	SER	373	26. 784 -20. 951	75. 457	1. 00 32. 56
	ATOM	2846	C	SER	373	26. 988 -17. 471	74. 034	1. 00 25. 31
	ATOM	2847	0	SER	373	27. 585 -17. 207	72. 998	1. 00 24. 49
	ATOM	2848	N	VAL	374	25. 962 -16. 754	74. 475	1. 00 25. 87
10	ATOM	2849	CA	VAL	374	25. 473 -15. 596	73. 743	1. 00 25. 12
	ATOM	2850	CB	VAL	374	24. 139 -15. 103	74. 319	1. 00 26. 07
	ATOM	2851	CG1	VAL	374	23. 754 -13. 766	73. 682	1. 00 29. 29
	ATOM	2852	CG2	VAL	374	23. 055 -16. 127	74. 061	1. 00 25. 56
	ATOM	2853	C	VAL	374	26. 465 -14. 429	73. 742	1. 00 24. 54
15	ATOM	2854	0	VAL	374	26. 657 -13. 792	72. 714	1. 00 25. 64
	ATOM	2855	N	SER	375	27. 094 -14. 144	74. 878	1. 00 21. 70
	ATOM	2856	CA	SER	375	28. 029 -13. 034	74. 922	1. 00 23. 89
	ATOM	2857	CB	SER	375	28. 298 -12. 585	76. 365	1. 00 23. 28
	ATOM	2858	0G	SER	375	28. 986 -13. 565	77. 120	1. 00 29. 71
20	ATOM	2859	C	SER	375	29. 324 -13. 391	74. 210	1. 00 24. 77
	ATOM	2860	0	SER	375	29. 873 -12. 560	73. 490	1. 00 23. 61
	ATOM	2861	N	THR	376	29. 805 -14. 623	74. 386	1. 00 23. 54
	ATOM	2862	CA	THR	376	31. 029 -15. 052	73. 707	1. 00 23. 38
	ATOM	2863	CB	THR	376	31. 444 -16. 501	74. 096	1. 00 23. 76
25	ATOM	2864	0G1	THR	376	31. 874 -16. 527	75. 458	1. 00 26. 36
	ATOM	2865	CG2	THR	376	32. 594 -16. 987	73. 222	1. 00 21. 48
	ATOM	2866	C	THR	376	30. 859 -14. 996	72. 189	1. 00 22. 33
	MOTA	2867	0	THR	376	31. 810 -14. 694	71. 465	1. 00 23. 88
	ATOM	2868	N	ARG	377	29. 660 -15. 293	71. 695	1. 00 20. 80

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	ATOM	2869	CA	ARG	377	29. 452 -15. 239	70. 253	1. 00 21. 46
	ATOM	2870	CB	ARG	377	28. 141 -15. 918	69. 839	1. 00 22. 21
	ATOM	2871	CG	ARG	377	27. 958 -15. 875	68. 312	1. 00 25. 01
	ATOM	2872	CD	ARG	377	26. 601 -16. 377	67. 827	1. 00 27. 70
5	ATOM	2873	NE	ARG	377	25. 491 -15. 558	68. 302	1. 00 25. 17
	ATOM	2874	CZ	ARG	377	24. 255 -15. 637	67. 825	1. 00 26. 42
	ATOM	2875	NH 1	ARG	377	23. 973 -16. 492	66. 850	1. 00 25. 23
	ATOM	2876	NH2	ARG	377	23. 294 -14. 877	68. 339	1. 00 26. 96
	ATOM	2877	C	ARG	377	29. 439 -13. 773	69. 787	1. 00 21. 55
10	MOTA	2878	0	ARG	377	29. 856 -13. 462	68. 670	1. 00 20. 80
	ATOM	2879	N	ALA	378	28. 951 -12. 879	70. 639	1. 00 19. 46
	ATOM	2880	CA	ALA	378	28. 927 -11. 463	70. 302	1. 00 21. 17
	ATOM	2881	CB	ALA	378	28. 239 -10. 653	71. 412	1. 00 20. 68
	ATOM	2882	C	ALA	378	30. 374 -11. 015	70. 151	1. 00 20. 18
15	ATOM	2883	0	ALA	378	30. 747 -10. 420	69. 145	1. 00 20. 36
	MOTA	2884	N	ALA	379	31. 191 -11. 326	71. 153	1. 00 19. 41
	ATOM	2885	CA	ALA	379	32. 600 -10. 950	71. 138	1. 00 20. 64
	ATOM	2886	CB	ALA	379	33. 296 -11. 515	72. 371	1. 00 20. 04
	ATOM	2887	C	ALA	379	33. 332 -11. 405	69. 869	1. 00 22. 79
20	ATOM	2888	0	ALA	379	34. 054 -10. 620	69. 234	1. 00 21. 82
	ATOM	2889	N	HIS	380	33. 139 -12. 666	69. 489	1. 00 22. 45
	ATOM	2890	CA	HIS	380	33. 803 -13. 208	68. 305	1. 00 22. 78
	ATOM	2891	CB	HIS	380	33. 726 -14. 745	68. 314	1. 00 22. 80
	ATOM	2892	CG	HIS	380	34. 584 -15. 384	69. 364	1. 00 26. 52
25	ATOM	2893	CD2	HIS	380	35. 557 -14. 870	70. 152	1. 00 27. 81
	ATOM	2894	ND1		380	34. 499 -16. 720	69. 687	1. 00 28. 99
	ATOM	2895	CE1	HIS	380	35. 383 -17. 002	70. 627	1. 00 28. 15
	ATOM	2896	NE2	HIS	380	36. 039 -15. 896	70. 927	1. 00 28. 70
	ATOM	2897	С	HIS	380	33. 242 -12. 657	66. 994	1. 00 22. 38

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	ATOM	2898	0	HIS	380	33. 988	-12. 368	66. 073	1. 00 20. 71
	ATOM	2899	N	MET	381	31. 926	-12. 524	66. 915	1. 00 23. 83
	ATOM	2900	CA	MET	381	31. 285	-12. 018	65. 713	1. 00 26. 66
	ATOM	2901	CB	MET	381	29. 760	-12. 086	65. 899	1. 00 29. 06
5	ATOM	2902	CG	MET	381	28. 926	-12. 031	64. 622	1. 00 34. 34
	ATOM	2903	SD	MET	381	29. 456	-13. 157	63. 312	1. 00 33. 69
	ATOM	2904	CE	MET	381	28. 228	-14. 472	63. 429	1. 00 34. 64
	ATOM	2905	C	MET	381	31. 781	-10. 580	65. 509	1. 00 27. 50
	ATOM	2906	0	MET	381	32. 153	-10. 188	64. 406	1. 00 26. 70
10	ATOM	2907	N	CYS	382	31. 830	-9. 813	66. 595	1. 00 26. 32
	ATOM	2908	CA	CYS	382	32. 302	-8. 441	66. 536	1. 00 24. 87
	ATOM	2909	CB	CYS	382	32. 102	-7. 769	67. 896	1. 00 26. 05
	ATOM	2910	SG	CYS	382	32. 389	-5. 962	67. 931	1. 00 26. 70
	ATOM	2911	C	CYS	382	33. 785	-8. 355	66. 122	1. 00 24. 60
15	ATOM	2912	0	CYS	382	34. 187	-7. 457	65. 360	1. 00 19. 92
	ATOM	2913	N	SER	383	34. 590	-9. 288	66. 623	1. 00 22. 62
	ATOM	2914	CA	SER	383	36. 017	-9. 302	66. 327	1. 00 22. 35
	ATOM	2915	CB	SER	383	36. 716	-10. 439	67. 096	1. 00 23. 03
	ATOM	2916	0G	SER	383	36. 361	-11. 712	66. 571	1. 00 24. 25
20	ATOM	2917	C	SER	383	36. 272	-9. 463	64. 834	1. 00 23. 77
	ATOM	2918	0	SER	383	37. 202	-8. 875	64. 288	1. 00 24. 79
	ATOM	2919	N	ALA	384	35. 448	-10. 269	64. 173	1. 00 24. 03
	ATOM	2920	CA	ALA	384	35. 612	-10. 480	62. 743	1. 00 25. 52
	ATOM	2921	CB	ALA	384	34. 649	-11. 552	62. 256	1. 00 22. 05
25	ATOM	2922	C	ALA	384	35. 369	-9. 182	61. 980	1. 00 25. 61
	ATOM	2923	0	ALA	384	35. 990	-8. 942	60. 947	1. 00 25. 37
	ATOM	2924	N	GLY	385	34. 450	-8. 360	62. 490	1. 00 25. 67
	ATOM	2925	CA	GLY	385	34. 134	-7. 098	61.842	1. 00 23. 86
	ATOM	2926	C	GLY	385	35. 289	-6. 128	61. 944	1. 00 20. 99

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	ATOM	2927	0	GLY	385		-5. 531	60. 960	1. 00 22. 47
	ATOM	2928	N	LEU	386	35. 811	-5. 962	63. 148	1. 00 22. 82
	ATOM	2929	CA	LEU	386	36. 937	-5. 065	63. 364	1. 00 25. 33
	ATOM	2930	CB	LEU	386	37. <u>2</u> 59	-4. 971	64. 850	1. 00 23. 48
5	ATOM	2931	CG	LEU	386	37. 800	-3. 658	65. 425	1. 00 27. 75
	ATOM	2932	CD1	LEU	386	38. 641	-4. 007	66. 641	1. 00 26. 18
	ATOM	2933	CD2	LEU	386	38. 621	-2. 865	64. 428	1. 00 25. 52
	ATOM	2934	C	LEU	386	38. 172	-5. 584	62. 616	1. 00 26. 01
	ATOM	2935	0	LEU	386	38. 953	-4. 794	62. 067	1. 00 26. 60
10	ATOM	2936	N	ALA	387	38. 356	-6. 904	62. 601	1. 00 23. 95
	ATOM	2937	CA	ALA	387	39. 509	-7. 482	61. 902	1. 00 24. 13
	ATOM	2938	CB	ALA	387	39. 585	-8. 989	62. 135	1. 00 20. 59
	ATOM	2939	C	ALA	387	39. 405	-7. 181	60. 411	1. 00 24. 07
	ATOM	2940	0	ALA	387	40. 419	-6. 990	59. 730	1. 00 22. 59
15	ATOM	2941	N	GLY	388	38. 175	-7. 141	59. 904	1. 00 24. 30
	ATOM	2942	CA	GLY	388	37. 975	-6. 838	58. 497	1. 00 24. 40
	ATOM	2943	C	GLY	388	38. 380	-5. 398	58. 203	1. 00 25. 62
	ATOM	2944	0.	GLY	388	39. 048	-5. 114	57. 205	1. 00 25. 24
	ATOM	2945	N	VAL	389	37. 974	-4. 488	59. 084	1. 00 25. 15
20	ATOM	2946	CA	VAL	389	38. 294	-3. 072	58. 950	1. 00 23. 08
	ATOM	2947	CB	VAL	389	37. 581	-2. 259	60. 057	1. 00 21. 38
	ATOM	2948	CG1	VAL	389	38. 083	-0. 820	60. 076	1. 00 21. 90
	ATOM	2949	CG2	VAL	389	36. 078	-2. 303	59. 819	1. 00 20. 64
	ATOM	2950	C	VAL	389	39. 802	-2. 858	59. 034	1. 00 24. 13
25	ATOM	2951	0	VAL	389	40. 402	-2. 198	58. 178	1. 00 25. 99
	ATOM	2952	N	ILE	390	40. 424	-3. 429	60. 054	1. 00 24. 21
	ATOM	2953	CA	ILE	390	41. 866	-3. 289	60. 209	1. 00 25. 31
	ATOM	2954	CB	ILE	390	42. 317	-3. 883	61. 576	1. 00 25. 21
	ATOM	2955	CG2	ILE	390	43. 831	-3. 962	61. 661	1. 00 27. 92

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	ATOM	2956	CG1	ILE	390	41. 778	-2. 993	62. 708	1. 00	26. 03
	ATOM	2957	CD1	ILE	390	42. 091	-3. 476	64. 094	1. 00	27. 41
	ATOM	2958	C	ILE	390	42. 668	-3. 899	59. 040	1. 00	26. 27
	ATOM	2959	0	ILE	390	43. 622	-3. 287	58. 563	1. 00	25. 08
5	ATOM	2960	N	ASN	391	42. 286	-5. 082	58. 561	1. 00	27. 72
	ATOM	2961	CA	ASN	391	43. 026	-5. 689	57. 448	1. 00	29. 87
	ATOM	2962	CB	ASN	391	42. 649	-7. 162	57. 250	1. 00	27. 74
	ATOM	2963	CG	ASN	391	43. 147	-8. 044	58. 375	1. 00	29. 54
	ATOM	2964	OD 1	ASN	391	44. 216	-7. 804	58. 939	1. 00	28. 68
10	ATOM	2965	ND2	ASN	391	42. 383	-9. 079	58. 699	1. 00	26. 84
	ATOM	2966	C	ASN	391	42. 805	-4. 930	56. 144	1. 00	31. 14
	ATOM	2967	0	ASN	391	43. 688	-4. 903	55. 281	1. 00	29. 49
	ATOM	2968	N	ARG	392	41. 627	-4. 331	55. 991	1. 00	31. 07
	ATOM	2969	CA	ARG	392	41. 358	-3. 553	54. 795	1. 00	33. 43
15	ATOM	2970	CB	ARG	392	39. 921	-3. 018	54. 780	1. 00	35. 04
	ATOM	2971	CG	ARG	392	39. 597	-2. 307	53. 483	1. 00	35. 84
	ATOM	2972	CD	ARG	392	38. 614	-1. 173	53. 650	1. 00	37. 18
	ATOM	2973	NE	ARG	392	38. 804	-0. 186	52. 589	1. 00	35. 89
	ATOM	2974	CZ	ARG	392	38. 518	-0. 390	51. 309	1. 00	36. 67
20	ATOM	2975	NH1	ARG	392	38. 006	-1. 550	50. 911	1. 00	38. 42
	ATOM	2976	NH2	ARG	392	38. 788	0. 553	50. 417	1. 00	37. 33
	ATOM	2977	C	ARG	392	42. 335	-2. 377	54. 831	1. 00	33. 73
	ATOM	2978	0	ARG	392	43. 028	-2. 107	53. 858	1. 00	34. 52
	ATOM	2979	N	MET	393	42. 396	-1. 691	55. 967	1. 00	34. 05
25	ATOM	2980	CA	MET	393	43. 298	-0. 554	56. 126	1. 00	35. 93
	ATOM	2981	CB	MET	393	43. 119	0. 073	57. 517	1. 00	32. 21
	ATOM	2982	CG	MET	393	41. 801	0. 834	57. 692	1. 00	28. 72
	ATOM	2983	SD	MET	393	41. 530	1. 348	59. 400	1. 00	27. 28
	ATOM	2984	CE	MET	393	42. 652	2. 753	59. 533	1. 00	24. 26

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	ATOM	2985	C	MET	393	44. 751	-0. 979	55. 947	1. 00 39. 48
	ATOM	2986	0	MET	393	45. 579	-0. 216	55. 448	1. 00 39. 63
	ATOM	2987	N	ARG	394	45. 049	-2. 205	56. 364	1. 00 43. 20
	ATOM	2988	CA	ARG	394	46. 391	-2. 766	56. 277	1. 00 45. 79
5	ATOM	2989	CB	ARG	394	46. 381	-4. 180	56. 870	1. 00 49. 86
	ATOM	2990	CG	ARG	394	47. 670	-4. 595	57. 551	1. 00 53. 76
	ATOM	2991	CD	ARG	394	48. 587	-5. 335	56. 612	1. 00 56. 09
	ATOM	2992	NE	ARG	394	49. 896	-5. 554	57. 217	1. 00 60. 36
	ATOM	2993	CZ	ARG	394	50. 797	-4. 596	57. 411	1. 00 60. 35
10	ATOM	2994	NH1	ARG	394	50. 528	-3. 353	57. 042	1. 00 61. 48
	ATOM	2995	NH2	ARG	394	51. 964	-4. 878	57. 978	1. 00 60. 51
	ATOM	2996	C	ARG	394	46. 912	-2. 792	54. 835	1. 00 46. 90
	ATOM	2997	0	ARG	394	48. 117	-2. 697	54. 606	1. 00 44. 95
	ATOM	2998	N	GLU	395	46. 005	-2. 906	53. 869	1. 00 48. 68
15	ATOM	2999	CA	GLU	395	46. 387	-2. 943	52. 459	1. 00 52. 84
	ATOM	3000	CB	GLU	395	45. 165	-3. 275	51. 590	1. 00 54. 51
	ATOM	3001	CG	GLU	395	44. 388	-4. 508	52. 051	1. 00 60. 85
	ATOM	3002	CD	GLU	395	43. 310	-4. 952	51.061	1. 00 64. 84
	ATOM	3003	0E1	GLU	395	42. 485	-4. 105	50. 642	1. 00 65. 83
20	ATOM	3004	0E2	GLU	395	43. 286	-6. 155	50. 708	1. 00 66. 43
	ATOM	3005	C	GLU	395	47. 008	-1. 621	51. 991	1. 00 54. 64
	ATOM	3006	0	GLU	395	47. 791	-1. 594	51. 039	1. 00 53. 71
	ATOM	3007	N	SER	396	46. 660	-0. 528	52. 666	1. 00 56. 54
	ATOM	3008	CA	SER	396	47. 179	0. 794	52. 313	1. 00 58. 22
25	ATOM	3009	CB	SER	396	46. 037	1. 808	52. 266	1. 00 57. 21
	ATOM	3010	0G	SER	396	44. 980	1. 340	51. 448	1. 00 59. 52
	ATOM	3011	C	SER	396	48. 221	1. 268	53. 318	1. 00 60. 22
	ATOM	3012	0	SER	396	48. 394	2. 468	53. 527	1. 00 60. 38
	ATOM	3013	N	ARG	397	48. 915	0. 324	53. 941	1. 00 62. 22

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	ATOM	3014	CA	ARG	397	49. 924	0. 663	54. 933	1. 00 64. 67
	ATOM	3015	CB	ARG	397	49. 430	0. 260	56. 324	1. 00 65. 24
	ATOM	3016	CG	ARG	397	49. 798	1. 218	57. 444	1. 00 67. 16
	ATOM	3017	CD	ARG	397	49. 178	2. 596	57. 244	1. 00 68. 03
5	ATOM	3018	NE	ARG	397	48. 803	3. 208	58. 516	1. 00 69. 13
	ATOM	3019	CZ	ARG	397	47. 681	2. 933	59. 178	1. 00 70. 58
	ATOM	3020	NH 1	ARG	397	46. 813	2. 059	58. 687	1. 00 71. 37
	ATOM	3021	NH2	ARG	397	47. 429	3. 521	60. 340	1. 00 70. 29
	ATOM	3022	C	ARG	397	51. 222	-0. 063	54. 611	1. 00 65. 54
10	ATOM	3023	0	ARG	397	51. 416	-1. 215	54. 998	1. 00 66. 75
	ATOM	3024	N	SER	398	52. 106	0. 621	53. 894	1. 00 66. 86
	ATOM	3025	CA	SER	398	53. 388	0. 052	53. 508	1. 00 67. 48
	ATOM	3026	CB	SER	398	53. 980	0. 832	52. 331	1. 00 67. 48
	ATOM	3027	0G	SER	398	53. 155	0. 725	51. 181	1. 00 66. 93
15	ATOM	3028	C	SER	398	54. 358	0. 063	54. 679	1. 00 68. 36
	ATOM	3029	0	SER	398	55. 036	1. 063	54. 934	1. 00 69. 35
	ATOM	3030	N	GLU	399	54. 413	-1. 059	55. 388	1. 00 67. 90
	ATOM	3031	CA	GLU	399	55. 297	-1. 206	56. 533	1. 00 68. 16
	ATOM	3032	CB	GLU	399	55. 002	-0. 126	57. 564	1. 00 68. 95
20	ATOM	3033	CG	GLU	399	53. 540	0. 020	57. 889	1. 00 71. 05
	ATOM	3034	CD	GLU	399	53. 261	1. 318	58. 598	1. 00 71. 37
	ATOM	3035	0E1	GLU	399	53. 871	1. 545	59. 662	1. 00 72. 25
	ATOM	3036	0E2	GLU	399	52: 443	2. 111	58. 089	1. 00 71. 32
	ATOM	3037	C	GLU	399	55. 167	-2. 581	57. 168	1. 00 67. 57
25	ATOM	3038	0	GLU	399	54. 078	-3. 155	57. 232	1. 00 67. 34
	ATOM	3039	N	ASP	400	56. 301	-3. 091	57. 635	1. 00 66. 86
	ATOM	3040	CA	ASP	400	56. 397	-4. 400	58. 265	1. 00 65. 75
	ATOM	3041	CB	ASP	400	57. 739	-4. 507	58. 989	1. 00 68. 55
	ATOM	3042	CG	ASP	400	58. 892	-3. 961	58. 157	1. 00 71. 49

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,	ATOM	3043	OD1	ASP	400	59. 015	-4. 356	56. 976	1. 00 72. 29
	ATOM	3044	OD2	ASP	400	59. 675	-3. 136	58. 682	1. 00 72. 38
	ATOM	3045	C	ASP	400	55. 247	-4. 676	59. 233	1. 00 63. 41
	ATOM	3046	0	ASP	400	54. 385	-5. 514	58. 962	1. 00 63. 27
5	ATOM	3047	N	VAL	401	55. 241	-3. 973	60. 361	1. 00 59. 50
	ATOM	3048	CA	VAL	401	54. 193	-4. 138	61. 360	1. 00 55. 59
	ATOM	3049	CB	VAL	401	54. 789	-4. 439	62. 757	1. 00 55. 81
	ATOM	3050	CG1	VAL	401	53. 698	-4. 375	63. 818	1. 00 54. 69
	ATOM	3051	CG2	VAL	401	55. 442	-5. 817	62. 757	1. 00 54. 18
10	ATOM	3052	C	VAL	401	53. 345	-2. 876	61. 454	1. 00 53. 78
	ATOM	3053	0	VAL	401	53. 841	-1. 807	61. 820	1. 00 53. 39
	ATOM	3054	N	MET	402	52. 065	-2. 991	61. 114	1. 00 50. 91
	ATOM	3055	CA	MET	402	51. 190	-1. 834	61. 194	1. 00 47. 59
	ATOM	3056	CB	MET	402	49. 992	-1. 958	60. 250	1. 00 46. 98
15	ATOM	3057	CG	MET	402	49. 043	-0. 768	60. 387	1. 00 47. 22
	ATOM	3058	SD	MET	402	47. 505	-0. 874	59. 461	1. 00 48. 69
	ATOM	3059	CE	MET	402	46. 622	-2. 099	60. 439	1. 00 48. 15
	ATOM	3060	C	MET	402	50. 670	-1. 643	62. 605	1. 00 44. 98
	ATOM	3061	0	MET	402	49. 945	-2. 483	63. 134	1. 00 43. 92
20	ATOM	3062	N	ARG	403	51.054	-0. 533	63. 219	1. 00 43. 27
	ATOM	3063	CA	ARG	403	50. 587	-0. 229	64. 556	1. 00 41. 71
	ATOM	3064	CB	ARG	403	51. 673	0. 484	65. 350	1. 00 45. 65
	ATOM	3065	CG	ARG	403	52. 903	-0. 356	65. 596	1. 00 52. 20
	ATOM	3066	CD	ARG	403	53. 973	0. 474	66. 262	1. 00 57. 99
25	ATOM	3067	NE	ARG	403	55. 137	-0. 324	66. 630	1. 00 65. 47
	ATOM	3068	CZ	ARG	403	56. 251	0. 184	67. 149	1. 00 68. 76
	ATOM	3069	NH1	ARG	403	56. 349	1. 493	67. 357	1. 00 69. 34
	ATOM	3070	NH2	ARG	403	57. 265	-0. 615	67. 468	1. 00 69. 59
	ATOM	3071	C	ARG	403	49. 388	0. 685	64. 372	1. 00 37. 99

- 122 -**ATOM** 3072 0 ARG 403 49. 471 1. 692 63. 679 1. 00 37. 13 ATOM 3073 N ILE 404 48. 267 64. 975 0.322 1. 00 34. 39 ATOM 3074 CAILE 404 47.069 64. 854 1. 129 1. 00 31. 53 ATOM 3075 CBILE 404 46. 161 0.577 63. 735 1. 00 33. 38 5 ATOM 3076 CG2 ILE 404 45. 681 -0.82964.096 1. 00 32. 57 ATOM 3077 CG1 ILE 404 44. 987 1. 524 63. 500 1. 00 35. 77 ATOM 3078 CD1 ILE 404 44. 144 1. 153 62. 300 1. 00 38. 45 3079 C ATOM ILE 404 46. 322 66. 179 1. 152 1. 00 28. 96 ATOM 3080 0 ILE 404 46. 393 66. 956 0. 204 1. 00 29. 35 10 ATOM 3081 N THR 405 45. 632 2. 250 66. 453 1.00 28.84 ATOM 3082 CA THR 405 44. 874 67. 693 2. 359 1. 00 27. 84 ATOM 3083 CB THR 405 45. 323 3. 558 68. 535 1. 00 26. 65 OG1 THR ATOM 3084 405 46.663 3. 335 68.990 1. 00 30. 48 **ATOM** 3085 CG2 THR 405 44. 428 3. 715 69. 749 1. 00 27. 32 ATOM 15 3086 C THR 405 43. 387 2. 460 67. 408 1. 00 27. 13 ATOM 3087 0 THR 405 42.964 3. 127 66. 462 1. 00 24. 36 ATOM 3088 N VAL 406 42.604 68. 245 1. 786 1. 00 25. 61 ATOM 3089 CA VAL 406 41. 160 1. 737 68. 107 1. 00 23. 67 ATOM 3090 CBVAL 406 40.705 0. 244 67. 973 1. 00 23. 64 20 ATOM 3091 CG1 VAL 406 39. 189 0. 138 67. 798 1. 00 24. 19 ATOM 3092 CG2 VAL 406 41. 405 -0.39966. 783 1.00 21.36 **ATOM** 3093 C VAL 406 40. 493 2. 392 69. 320 1. 00 26. 21 **ATOM** 3094 0 VAL 406 40. 763 ² 2. 018 70. 469 1. 00 26. 86 **ATOM** 3095 N GLY 407 39. 644 3. 389 69.072 1. 00 25. 61 ATOM 25 3096 CA GLY 407 38. 943 4. 044 70. 168 1. 00 23. 09 ATOM C 3097 GLY 407 37. 645 3. 285 70. 387 1.00 21.77 ATOM 3098 0 GLY 407 36. 919 3.011 69. 426 1. 00 23. 17 **ATOM** 3099 N VAL 408 37. 334 2. 943 71.632 1. 00 20. 52

ATOM

3100

CA

VAL

408

36. 128

2. 167

71. 907

1.00 21.51

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	ATOM	3101	CB	VAL	408	36. 500	0. 684	72. 252	1. 00 23. 04
	ATOM	3102	CG1	VAL	408	35. 237	-0. 176	72. 351	1. 00 19. 52
	ATOM	3103	CG2	VAL	408	37. 436	0. 121	71. 201	1. 00 20. 49
	ATOM	3104	C	VAL	408	35. 282	2. 704	73. 060	1. 00 23. 66
5	ATOM	3105	0	VAL	408	35. 814	3. 223	74. 045	1. 00 23. 60
	ATOM	3106	N	ASP	409	33. 963	2. 580	72. 923	1. 00 24. 58
	ATOM	3107	CA	ASP	409	33. 040	2. 992	73. 975	1. 00 26. 70
	ATOM	3108	CB	ASP	409	32. 612	4. 455	73. 803	1. 00 30. 78
	ATOM	3109	CG	ASP	409	31. 909	4. 998	75. 041	1. 00 31. 51
10	ATOM	3110	0D1	ASP	409	32. 322	4. 625	76. 156	1. 00 31. 70
	ATOM	3111	OD2	ASP	409	30. 955	5. 794	74. 910	1. 00 35. 70
	ATOM	3112	C	ASP	409	31. 824	2. 083	73. 898	1. 00 25. 68
	ATOM	3113	0	ASP	409	31. 639	1. 396	72. 901	1. 00 27. 99
	ATOM	3114	N	GLY	410	30. 999	2. 079	74. 943	1. 00 28. 67
15	ATOM	3115	CA	GLY	410	29. 807	1. 233	74. 964	1. 00 29. 54
	ATOM	3116	C	GLY	410	29. 755	0. 355	76. 212	1. 00 30. 09
	ATOM	3117	Ó	GLY	410	30. 787	-0. 138	76. 657	1. 00 28. 57
	ATOM	3118	N	SER	411	28. 560	0. 150	76. 767	1. 00 30. 89
	ATOM	3119	CA	SER	411	28. 392	-0. 649	77. 983	1. 00 32. 71
20	ATOM	3120	CB	SER	411	26. 941	-0. 554	78. 490	1. 00 32. 88
	ATOM	3121	0G	SER	411	26. 011	-0. 884	77. 473	1. 00 36. 82
	ATOM	3122	C	SER	411	28. 804	-2. 121	77. 840	1. 00 31. 25
	ATOM	3123	0	SER	411	29. 480	-2. 661	78. 712	1. 00 29. 96
	ATOM	3124	N	VAL	412	28. 398	-2. 768	76. 754	1. 00 29. 78
25	ATOM	3125	CA	VAL	412	28. 780	-4. 158	76. 535	1. 00 28. 59
	ATOM	3126	CB	VAL	412	28. 264	-4. 665	75. 174	1. 00 29. 68
	ATOM	3127	CG1	VAL	412	28. 772	-6. 088	74. 908	1. 00 27. 25
	ATOM	3128	CG2	VAL	412	26. 739	-4. 642	75. 173	1. 00 29. 93
	ATOM	3129	C	VAL	412	30. 307	-4. 320	76. 584	1. 00 29. 24

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	ATOM	3130	0	VAL	412	30. 831	-5. 145	77. 340	1. 00 28. 78
	ATOM	3131	N	TYR	413	31. 023	-3. 522	75. 796	1. 00 27. 57
	ATOM	3132	CA	TYR	413	32. 482	-3. 602	75. 763	1. 00 24. 60
	ATOM	3133	CB	TYR	413	33. 049	-2. 730	74. 645	1. 00 19. 87
5	ATOM	3134	CG	TYR	413	34. 568	-2. 710	74. 587	1. 00 20. 22
	ATOM	3135	CD	1 TYR	413	35. 270	-3. 566	73. 735	1. 00 21. 52
	ATOM	3136	CE	1 TYR	413	36. 667	-3. 519	73. 655	1. 00 19. 93
	ATOM	3137	CD	2 TYR	413	35. 300	-1. 819	75. 363	1. 00 14. 63
	ATOM	3138	CE	2 TYR	413	36. 690	-1. 770	75. 294	1. 00 17. 31
10	ATOM	3139	CZ	TYR	413	37. 364	-2. 616	74. 439	1. 00 19. 92
	ATOM	3140	ОН	TYR	413	38. 737	-2. 547	74. 362	1. 00 23. 08
	ATOM	3141	C	TYR	413	33. 151	-3. 193	77. 072	1. 00 26. 48
	ATOM	3142	0	TYR	413	34. 085	-3. 849	77. 534	1. 00 26. 86
	ATOM	3143	N	LYS	414	32. 690	-2. 108	77. 669	1. 00 26. 13
15	ATOM	3144	CA	LYS	414	33. 309	-1. 640	78. 902	1. 00 29. 80
	ATOM	3145	CB	LYS	414	33. 001	-0. 147	79. 117	1. 00 29. 42
	ATOM	3146	CG	LYS	414	33. 882	0. 802	78. 302	1. 00 32. 94
	ATOM	3147	CD	LYS	414	33. 558	2. 275	78. 559	1. 00 34. 12
	ATOM	3148	CE	LYS	414	34. 553	3. 179	77. 833	1. 00 36. 09
20	ATOM	3149	NZ	LYS	414	34. 170	4. 626	77. 859	1. 00 35. 28
	ATOM	3150	С	LYS	414	32. 966	-2. 400	80. 181	1. 00 29. 74
	ATOM	3151	0	LYS	414	33. 850	-2. 677	80. 988	1. 00 28. 77
	ATOM	3152	N	LEU	415	31. 696	-2. 749	80. 357	1. 00 30. 99
	ATOM	3153	CA	LEU	415	31. 255	-3. 395	81. 591	1. 00 34. 39
25	ATOM	3154	CB	LEU	415	29. 942	-2. 738	82. 041	1. 00 34. 94
	ATOM	3155	CG	LEU	415	29. 964	-1. 195	82. 012	1. 00 38. 17
	ATOM	3156	CD1	LEU	415	28. 610	-0. 647	82. 469	1. 00 38. 59
	ATOM	3157	CD2	LEU	415	31. 080	-0. 660	82. 901	1. 00 34. 42
	ATOM	3158	C	LEU	415	31. 113	-4. 923	81. 657	1. 00 34. 46

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	ATOM	3159	0	LEU	415	31. 202	-5. 493	82. 741	1. 00 33. 89
	ATOM	3160	N	HIS	416	30. 886	-5. 586	80. 531	1. 00 34. 56
	ATOM	3161	CA	HIS	416	30. 746	-7. 041	80. 561	1. 00 36. 94
	ATOM	3162	CB	HIS	416	30. 394	-7. 572	79. 175	1. 00 39. 81
5	ATOM	3163	CG	HIS	416	29. 811	-8. 949	79. 192	1. 00 44. 04
	ATOM	3164	CD	2 HIS	416	28. 536	-9. 375	79. 038	1. 00 43. 02
	ATOM	3165	ND	1 HIS	416	30. 573 -	10. 080	79. 402	1. 00 44. 57
	MOTA	3166	CE	1 HIS	416	29. 791 -	11. 144	79. 374	1. 00 44. 76
	ATOM	3167	NE:	2 HIS	416	28. 550 -	10. 744	79. 156	1. 00 46. 14
10	ATOM	3168	C	HIS	416	32. 046	-7. 673	81. 060	1. 00 35. 57
	ATOM	3169	0	HIS	416	33. 103 -	-7. 483	80. 471	1. 00 37. 06
	ATOM	3170	N	PRO	417	31. 973 -	-8. 445	82. 153	1. 00 33. 55
	ATOM	3171	CD	PRO	417	30. 727 -	-8. 999	82. 700	1. 00 32. 04
	ATOM	3172	CA	PRO	417	33. 134 -	-9. 109	82. 757	1. 00 33. 47
15	MOTA	3173	CB	PRO	417	32. 504 -1	10. 219	83. 614	1. 00 31. 67
	ATOM	3174	CG	PRO	417	31. 142 -1	0. 410	83. 016	1. 00 32. 88
	ATOM	3175	C	PRO	417	34. 252 -	9. 628	81. 849	1. 00 32. 70
	ATOM	3176	0	PR0	417	35. 428 -	9. 411	82. 146	1. 00 36. 28
	ATOM	3177	N	SER	418	33. 929 -1	0. 302	80. 752	1. 00 29. 70
20	ATOM	3178	CA	SER	418	35. 015 -1	0. 808	79. 915	1. 00 28. 37
	ATOM	3179	CB	SER	418	35. 215 -1	2. 314	80. 163	1. 00 30. 65
	MOTA	3180	0G	SER	418	35. 798 -1	2. 555	81. 439	1. 00 35. 61
	ATOM	3181	C	SER	418	34. 895 -1	0. 560	78. 418	1. 00 25. 27
	ATOM	3182	0	SER	418	35. 730 -1	1. 028	77. 648	1. 00 23. 69
25	ATOM	3183	N	PHE	419	33. 856 -	9. 846	78. 004	1. 00 21. 86
	ATOM	3184	CA	PHE	419	33. 673	9. 543	76. 587	1. 00 24. 13
	ATOM	3185	CB	PHE	419	32. 551 -	8. 522	76. 407	1. 00 22. 03
	ATOM	3186	CG	PHE	419	32. 270 -	8. 187	74. 978	1. 00 24. 42
	ATOM	3187	CD1	PHE	419	31. 273 -8	8. 860	74. 276	1. 00 23. 32

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	ATOM	3188	CD2	PHE	419	33. 033 -7. 23	1 74. 312	1. 00 22. 16
	ATOM	3189	CE1	PHE	419	31. 038 -8. 59	3 72. 932	1. 00 23. 49
	ATOM	3190	CE2	PHE	419	32. 808 -6. 96	1 72. 967	1. 00 25. 91
	ATOM	3191	CZ	PHE	419	31. 806 -7. 64	5 72. 275	1. 00 24. 70
5	ATOM	3192	C	PHE	419	34. 961 -8. 96	5 76. 000	1. 00 24. 09
	ATOM	3193	0	PHE	419	35. 491 -9. 45	5 75. 009	1. 00 26. 51
	ATOM	3194	N	LYS	420	35. 432 -7. 89	9 76. 628	1. 00 25. 00
	ATOM	3195	CA	LYS	420	36. 641 -7. 17	9 76. 238	1. 00 26. 79
	ATOM	3196	CB	LYS	420	36. 984 -6. 20	7 77. 370	1. 00 28. 35
10	ATOM	3197	CG	LYS	420	38. 241 -5. 39	6 77. 229	1. 00 30. 04
	ATOM	3198	CD	LYS	420	38. 433 -4. 53	78. 497	1. 00 33. 98
•	ATOM	3199	CE	LYS	420	37. 170 -3. 74	0 78. 832	1. 00 31. 09
	ATOM	3200	NZ	LYS	420	37. 322 -2. 92	3 80. 067	1. 00 36. 69
	ATOM	3201	C	LYS	420	37. 819 -8. 11	8 75. 968	1. 00 25. 76
15	ATOM	3202	0	LYS	420	38. 446 -8. 06	4 74. 911	1. 00 25. 94
	ATOM	3203	N	GLU	421	38. 111 -8. 96	76. 951	1. 00 24. 13
	ATOM	3204	CA	GLU	421	39. 195 -9. 92	9 76. 887	1. 00 26. 26
	ATOM	3205	CB	GLU	421	39. 204 -10. 78	1 78. 155	1. 00 32. 38
	ATOM	3206	CG	GLU	421	39. 547 -10. 043	3 79.417	1. 00 38. 45
20	ATOM	3207	CD	GLU	421	38. 700 -8. 798	3 79.664	1. 00 41. 54
	ATOM	3208	0E1	GLU	421	37. 458 -8. 844	4 79. 501	1. 00 42. 17
	ATOM	3209	0E2	GLU	421	39. 300 -7. 76	7 80. 053	1. 00 42. 62
	ATOM	3210	C	GLU	421	39. 075 -10. 864	75. 699	1. 00 24. 57
	ATOM	3211	0	GLU	421	40. 017 -11. 023	3 74. 930	1. 00 25. 86
25	ATOM	3212	N	ARG	422	37. 921 -11. 509	75. 576	1. 00 24. 00
	ATOM	3213	CA	ARG	422	37. 682 -12. 439	74. 480	1. 00 26. 01
	ATOM	3214	CB	ARG	422	36. 284 -13. 063	74. 610	1. 00 27. 36
	ATOM	3215	CG	ARG	422	36. 076 -13. 878	75. 887	1. 00 31. 58
	ATOM	3216	CD	ARG	422	34. 600 -14. 053	76. 188	1. 00 35. 39

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	ATOM	3217	NE	ARG	422	34. 390	-14. 834	77. 397	1. 00	40. 58
	ATOM	3218	CZ	ARG	422	33. 232	-14. 911	78. 046	1. 00	44. 53
	ATOM	3219	NH1	ARG	422	32. 171	-14, 243	77. 596	1. 00	41. 79
	ATOM	3220	NH2	ARG	422	33. 141	-15. 651	79. 150	1. 00	41. 67
5	ATOM	3221	C	ARG	422	37. 794	-11. 691	73. 160	1. 00	24. 48
	ATOM	3222	0	ARG	422	38. 439	-12. 148	72. 221	1. 00	22. 97
	ATOM	3223	N	PHE	423	37. 153	-10. 531	73. 094	1. 00	24. 48
	ATOM	3224	CA	PHE	423	37. 189	-9. 737	71. 879	1. 00	22. 97
	ATOM	3225	CB	PHE	423	36. 403	-8. 442	72. 089	1. 00	24. 98
10	ATOM	3226	CG	PHE	423	36. 494	-7. 484	70. 939	1. 00	25. 21
	ATOM	3227	CD1	PHE	423	37. 468	-6. 490	70. 926	1. 00	25. 04
	ATOM	3228	CD2	PHE	423	35. 618	-7. 584	69. 861	1. 00	23. 47
	ATOM	3229	CE1	PHE	423	37. 568	-5. 607	69. 857	1. 00	24. 77
	ATOM	3230	CE2	PHE	423	35. 710	-6. 708	68. 784	1. 00	25. 48
15	ATOM	3231	CZ	PHE	423	36. 684	-5. 715	68. 780	1. 00	24. 31
	ATOM	3232	C	PHE	423	38. 629	-9. 442	71. 456	1. 00	21. 03
	ATOM	3233	0	PHE	423	38. 989	-9. 680	70. 308	1. 00	19. 38
	ATOM	3234	N	HIS	424	39. 454	-8. 952	72. 381	1. 00	20. 46
	ATOM	3235	CA	HIS	424	40. 846	-8. 631	72. 054	1. 00	23. 40
20	ATOM	3236	CB	HIS	424	41. 602	-8. 128	73. 293	1. 00	24. 89
	ATOM	3237	CG	HIS	424	41. 133	-6. 803	73. 808	1. 00	25. 28
	ATOM	3238	CD2	HIS	424	40. 391	-5. 828	73. 230	1. 00	24. 67
	ATOM	3239	ND1	HIS	424	41. 419	-6. 361	75. 083	1. 00	25. 18
	ATOM	3240	CE1	HIS	424	40. 869	-5. 174	75. 269	1. 00	22. 64
25	ATOM	3241	NE2	HIS	424	40. 239	-4. 829	74. 161	1. 00 2	24. 12
	ATOM	3242	C	HIS	424	41. 604	-9. 834	71. 486	1. 00 2	24. 51
	ATOM	3243	0	HIS	424	42. 239	-9. 741	70. 432	1. 00 2	23. 58
	ATOM	3244	N	ALA	425	41. 540	-10. 962	72. 191	1. 00 2	24. 51
	ATOM	3245	CA	ALA	425	42. 242	-12. 164	71. 746	1. 00 2	26. 94

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	ATOM	3246	CB	ALA	425	42. 068 -13. 306	72. 774	1. 00 27. 10
	ATOM	3247	C	ALA	425	41. 759 -12. 605	70. 370	1. 00 25. 71
	ATOM	3248	0	ALA	425	42. 559 -12. 937	69. 505	1. 00 27. 02
	ATOM	3249	N	SER	426	40. 453 -12. 600	70. 151	1. 00 24. 30
5	ATOM	3250	CA	SER	426	39. 967 -13. 003	68. 850	1. 00 23. 93
	ATOM	3251	CB	SER	426	38. 450 -13. 142	68. 863	1. 00 20. 85
	ATOM	3252	0G	SER	426	38. 007 -13. 582	67. 596	1. 00 21. 86
	ATOM	3253	C	SER	426	40. 394 -12. 039	67. 743	1. 00 25. 72
	ATOM	3254	0	SER	426	40. 760 -12. 483	66. 660	1. 00 25. 40
10	ATOM	3255	N	VAL	427	40. 363 -10. 727	68. 007	1. 00 27. 03
	ATOM	3256	CA	VAL	427	40. 761 -9. 750	66. 983	1. 00 27. 43
	MOTA	3257	CB	VAL	427	40. 591 -8. 269	67. 450	1. 00 28. 91
	ATOM	3258	CG1	VAL	427	40. 999 -7. 323	66. 314	1. 00 29. 57
	ATOM	3259	CG2	VAL	427	39. 150 -7. 990	67. 852	1. 00 27. 73
15	ATOM	3260	C	VAL	427	42. 226 -9. 919	66. 601	1. 00 28. 67
	ATOM	3261	0	VAL	427	42. 582 -9. 858	65. 424	1. 00 27. 30
	ATOM	3262	N	ARG	428	43. 076 -10. 119	67. 603	1. 00 28. 43
	ATOM	3263	CA	ARG	428	44. 498 -10. 281	67. 350	1. 00 31. 91
	ATOM	3264	CB	ARG	428	45. 273 -10. 231	68. 670	1. 00 31. 80
20	ATOM	3265	CG	ARG	428	45. 449 -8. 793	69. 130	1. 00 31. 90
	ATOM	3266	CD	ARG	428	45. 662 -8. 639	70. 617	1. 00 34. 40
	ATOM	3267	NE	ARG	428	45. 867 -7. 231	70. 971	1. 00 34. 78
	ATOM	3268	CZ	ARG	428	45. 668 -6. 728	72. 186	1. 00 38. 69
	ATOM	3269	NH1	ARG	428	45. 251 -7. 516	73. 172	1. 00 38. 56
25	ATOM	3270	NH2	ARG	428	45. 901 -5. 442	72. 424	1. 00 39. 08
	ATOM	3271	C	ARG	428	44. 797 -11. 548	66. 572	1. 00 33. 56
	ATOM	3272	0	ARG	428	45. 694 -11. 558	65. 731	1. 00 32. 81
	ATOM	3273	N	ARG	429	44. 037 -12. 609	66. 837	1. 00 34. 25
	MOTA	3274	CA	ARG	429	44. 224 -13. 859	66. 115	1. 00 33. 42

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	ATOM	3275	CB	ARG	429	43. 252 -14. 941	66. 601	1. 00 36. 36
	ATOM	3276	CG	ARG	429	43. 756 -15. 769	67. 760	1. 00 43. 73
	ATOM	3277	CD	ARG	429	42. 930 -17. 038	67. 939	1. 00 47. 67
	ATOM	3278	NE	ARG	429	41. 561 -16. 789	68. 398	1. 00 51. 58
5	ATOM	3279	CZ	ARG	429	41. 222 -16. 467	69. 646	1. 00 51. 70
	ATOM	3280	NH1	ARG	429	42. 154 -16. 345	70. 585	1. 00 50. 85
	ATOM	3281	NH2	ARG	429	39. 945 -16. 288	69. 962	1. 00 49. 95
	ATOM	3282	C	ARG	429	43. 960 -13. 618	64. 639	1. 00 32. 81
	ATOM	3283	0	ARG	429	44. 610 -14. 215	63. 783	1. 00 32. 29
10	ATOM	3284	N	LEU	430	43. 001 -12. 741	64. 345	1. 00 30. 18
	ATOM	3285	CA	LEU	430	42. 623 -12. 455	62. 965	1. 00 29. 19
	ATOM	3286	CB	LEU	430	41. 132 -12. 109	62. 904	1. 00 29. 15
	ATOM	3287	CG	LEU	430	40. 173 -13. 164	63. 453	1. 00 31. 83
	ATOM	3288	CD1	LEU	430	38. 746 -12. 629	63. 437	1. 00 28. 32
15	ATOM	3289	CD2	LEU	430	40. 281 -14. 441	62. 613	1. 00 32. 03
	ATOM	3290	C	LEU	430	43. 407 -11. 355	62. 251	1. 00 27. 64
	ATOM	3291	0	LEU	430	43. 244 -11. 151	61. 048	1. 00 28. 08
	ATOM	3292	N	THR	431	44. 261 -10. 645	62. 966	1. 00 28. 04
	ATOM	3293	CA	THR	431	44. 988 -9. 567	62. 326	1. 00 31. 15
20	ATOM	3294	CB	THR	431	44. 569 -8. 201	62. 934	1. 00 30. 03
	ATOM	3295	0G1	THR	431	44. 666 -8. 254	64. 363	1. 00 31. 84
	ATOM	3296	CG2	THR	431	43. 137 -7. 879	62. 561	1. 00 26. 93
	ATOM	3297	C	THR	431	46. 507 -9. 719	62. 367	1. 00 34. 65
	ATOM	3298	0	THR	431	47. 190 -9. 015	63. 101	1. 00 34. 08
25	ATOM	3299	N	PR0	432	47. 049 -10. 655	61. 566	1. 00 37. 36
	ATOM	3300	CD	PR0	432	46. 296 -11. 603	60. 726	1. 00 37. 91
	ATOM	3301	CA	PR0	432	48. 489 -10. 923	61. 484	1. 00 38. 59
	ATOM	3302	CB	PRO	432	48. 572 -12. 080	60. 487	1. 00 38. 98
	ATOM	3303	CG	PRO	432	47. 245 -12. 758	60. 630	1. 00 40. 10

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	ATOM	3304	C	PR0	432	49. 224	-9. 689	60. 969	1. 00 39. 65
	ATOM	3305	0	PRO	432	48. 712	-8. 968	60. 113	1. 00 39. 80
	ATOM	3306	N	SER	433	50. 420	-9. 461	61. 495	1. 00 39. 94
	ATOM	3307	CA	SER	433	51. 254	-8. 326	61. 112	1. 00 42. 47
5	ATOM	3308	CB	SER	433	51. 467	-8. 280	59. 586	1. 00 44. 12
	ATOM	3309	0G	SER	433	50. 363	-7. 707	58. 898	1. 00 48. 10
	ATOM	3310	C	SER	433	50. 687	-6. 996	61. 598	1. 00 42. 26
	ATOM	3311	0	SER	433	51. 085	-5. 932	61. 121	1. 00 42. 50
	ATOM	3312	N	CYS	434	49. 756	-7. 053	62. 544	1. 00 40. 68
10	ATOM	3313	CA	CYS	434	49. 184	-5. 831	63. 092	1. 00 40. 64
	ATOM	3314	CB	CYS	434	47. 679	-5. 735	62. 826	1. 00 39. 36
	ATOM	3315	SG	CYS	434	47. 196	-5. 674	61. 111	1. 00 39. 36
	ATOM	3316	C	CYS	434	49. 398	-5. 789	64. 590	1. 00 40. 17
	ATOM	3317	0	CYS	434	49. 258	-6. 801	65. 281	1. 00 40. 51
15	ATOM	3318	N	GLU	435	49. 743	-4. 609	65. 081	1. 00 38. 91
	ATOM	3319	CA	GLU	435	49. 945	-4. 388	66. 504	1. 00 39. 30
	ATOM	3320	CB	GLU	435	51. 302	-3. 733	66. 738	1. 00 42. 29
	ATOM	3321	CG	GLU	435	51. 779	-3. 766	68. 162	1. 00 49. 24
	ATOM	3322	CD	GLU	435	53. 072	-2. 993	68. 340	1. 00 53. 77
20	ATOM	3323	0E1	GLU	435	54. 106	-3. 421	67. 781	1. 00 56. 24
	ATOM	3324	0E2	GLU	435	53. 047	-1. 950	69. 032	1. 00 54. 88
	ATOM	3325	C	GLU	435	48. 801	-3. 430	66. 839	1. 00 37. 06
	ATOM	3326	0	GLU	435	48. 866	-2. 241	66. 532	1. 00 34. 30
	ATOM	3327	N	ILE	436	47. 749	-3. 971	67. 449	1. 00 36. 39
25	ATOM	3328	CA	ILE	436	46. 552	-3. 203	67. 786	1. 00 34. 47
	ATOM	3329	CB	ILE	436	45. 280	-4. 040	67. 508	1. 00 34. 15
	ATOM	3330	CG2	ILE	436	44. 024	-3. 166	67. 639	1. 00 33. 64
	ATOM	3331	CG1	ILE	436	45. 357	-4. 633	66. 100	1. 00 36. 06
	ATOM	3332	CD1	ILE	436	44. 166	-5. 487	65. 719	1. 00 36. 35

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ATOM 3333 C ILE 436 46. 492 -2. 717 69. 228 1. 00 34. 50 ATOM 3334 0 ILE 436 46. 612 -3. 506 70. 164 1. 00 35. 88 3335 ATOM N THR 437 46. 308 -1.41169. 405 1. 00 32. 66 ATOM 3336 CA THR 437 46. 196 -0.837 70. 741 1. 00 30. 32 ATOM 3337 CBTHR 5 437 47. 134 70. 930 0.370 1. 00 29. 83 ATOM 3338 OG1 THR 437 48. 496 -0.06070. 833 1. 00 33. 74 ATOM 3339 CG2 THR 437 46. 925 0.996 72. 294 1. 00 28. 96 ATOM 3340 C THR -0.377437 44. 759 70. 949 1. 00 29. 92 **ATOM** 3341 0 THR 437 44. 177 0. 293 70.090 1. 00 28. 24 ATOM 3342 N PHE 10 438 44. 179 -0.75072.083 1. 00 29. 43 ATOM 3343 CA PHE 438 72. 390 42. 807 -0.3591. 00 29. 35 **ATOM** 3344 CBPHE 438 41. 991 -1.56772. 853 1. 00 27. 92 ATOM 3345 CG PHE 438 41. 794 -2.61471. 789 1. 00 27. 95 ATOM 3346 CD1 PHE 438 42. 695 -3.66171.648 1. 00 27. 90 15 ATOM 3347 CD2 PHE 438 40. 703 -2.54970.930 1. 00 24. 76 ATOM 3348 CE1 PHE 438 42. 505 -4.63470.662 1. 00 29. 21 CE2 PHE ATOM 3349 438 40. 506 -3.50569. 950 1. 00 28. 87 **ATOM** 3350 CZ PHE 438 41. 408 -4.55469.814 1. 00 28. 70 ATOM 3351 C PHE 438 42. 772 73. 467 0.712 1. 00 30. 41 **ATOM** 3352 0 PHE 20 438 43. 469 0.601 74. 474 1. 00 30. 53 **ATOM** 3353 N ILE 41.968 439 1. 752 73. 250 1. 00 30. 35 ATOM 3354 CA ILE 41.839 439 2.832 74. 220 1. 00 31. 89 ATOM 3355 CB ILE 439 42. 544 4. 124 73. 751 1. 00 33. 03 ATOM 3356 CG2 ILE 439 42. 233 74. 721 5. 269 1. 00 36. 00 ATOM 25 3357 CG1 ILE 439 44. 053 3. 916 73. 704 1. 00 33. 82 ATOM 3358 CD1 ILE 439 44. 818 5. 165 73. 296 1. 00 36. 93 ATOM 3359 C ILE 439 40. 373 3. 158 74. 420 1. 00 32. 85 ATOM 3360 0 ILE 439 39. 603 3. 157 73. 467 1. 00 33. 09 ATOM 3361 N GLU 440 39. 991 3. 442 75. 659 1. 00 35. 09

- 132 -ATOM 3362 CA GLU 440 38. 608 3. 789 75. 956 1.00 39.34 ATOM 3363 CB GLU 440 38. 133 3. 041 77. 199 1. 00 37. 95 **ATOM** 3364 CG GLU 440 38. 213 1. 526 77. 038 1. 00 39. 96 ATOM 3365 CD GLU 440 37.837 0.773 78. 298 1. 00 40. 82 5 ATOM 3366 OE1 GLU 440 38. 058 -0.45678. 340 1. 00 41. 23 ATOM 3367 OE2 GLU 79. 245 440 37. 318 1. 403 1.00 41.08 ATOM 3368 C GLU 76. 156 440 38. 495 5. 298 1. 00 41. 28 **ATOM** 3369 0 GLU 440 39. 356 5. 918 76. 769 1. 00 42. 10 ATOM 3370 N SER 441 37. 431 75.627 5. 886 1. 00 43. 99 10 ATOM 3371 CA SER 441 37. 231 7. 327 75. 738 1. 00 48. 53 ATOM 3372 CB SER 441 36. 390 7. 823 74. 550 1. 00 47. 96 **ATOM** 3373 0G SER 441 35. 196 7.066 74. 390 1. 00 48. 42 ATOM 3374 C SER 441 36. 577 7. 752 77. 051 1. 00 50. 20 ATOM 3375 0 SER 441 35. 654 7.087 77. 531 1. 00 51. 01 15 ATOM 3376 N GLU 442 37. 060 8. 852 77. 634 1. 00 53. 24 ATOM 3377 CA GLU 442 36. 490 9. 359 78. 885 1. 00 55. 51 ATOM 3378 CB GLU 442 37. 362 10. 454 79. 507 1. 00 60. 16 ATOM 3379 CG GLU 442 36. 822 10. 936 80. 859 1. 00 65. 44 **ATOM** 3380 CD GLU 442 37. 596 12. 107 81. 450 1.00 69.63 20 **ATOM** 3381 OE1 GLU 442 38.824 11. 984 81. 667 1. 00 71. 27 **ATOM** 3382 OE2 GLU 442 36. 965 13. 155 81.709 1. 00 72. 91 ATOM 3383 C GLU 442 35. 118 9.938 78. 579 1.00 54.68 **ATOM** 3384 0 GLU 442 34. 104 9. 495 79. 126 1. 00 56. 30 ATOM 3385 N GLU 443 35. 094 10.942 77. 714 1. 00 51. 73 25 ATOM 3386 CA GLU 443 33. 840 11. 555 77. 307 1. 00 51. 12 ATOM 3387 CBGLU 443 33. 706 12.960 77.888 1. 00 51. 77 ATOM 3388 CG GLU 443 32. 561 13. 086 78.869 1.00 49.05 **ATOM** CD 3389 GLU 443 31. 202 12. 812 78. 239 1. 00 48. 41

ATOM

3390

OE1 GLU

443

30. 245

12. 572

79.006

1. 00 48. 06

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	ATOM	3391	0E2	GLU	443	31. 084	12. 842	76. 990	1. 00 44. 46
	ATOM	3392	C	GLU	443	33. 851	11. 614	75. 793	1. 00 50. 48
	ATOM	3393	0	GLU	443	33. 624	12. 662	75. 191	1. 00 50. 61
	ATOM	3394	N	GLY	444	34. 131	10. 458	75. 199	1. 00 49. 69
5	ATOM	3395	CA	GLY	444	34. 213	10. 321	73. 760	1. 00 46. 29
	ATOM	3396	C	GLY	444	33. 300	11. 190	72. 928	1. 00 45. 39
	ATOM	3397	0	GLY	444	33. 786	12. 031	72. 181	1. 00 44. 10
	ATOM	3398	N	SER	445	31. 990	10. 996	73. 052	1. 00 44. 40
	ATOM	3399	CA	SER	445	31. 035	11. 765	72. 263	1. 00 45. 82
10	ATOM	3400	CB	SER	445	29. 614	11. 258	72. 505	1. 00 43. 70
	ATOM	3401	0G	SER	445	29. 248	11. 396	73. 860	1. 00 51. 13
	ATOM	3402	C	SER	445	31. 108	13. 265	72. 523	1. 00 45. 79
	ATOM	3403	0	SER	445	31. 381	14. 043	71. 607	1. 00 46. 62
	ATOM	3404	N	GLY	446	30. 867	13. 666	73. 766	1. 00 45. 46
15	ATOM	3405	CA	GLY	446	30. 924	15. 075	74. 112	1. 00 44. 61
	ATOM	3406	C	GLY	446	32. 176	15. 778	73. 615	1. 00 44. 65
	ATOM	3407	0	GLY	446	32. 085	16. 754	72. 872	1. 00 45. 17
	ATOM	3408	N	ARG	447	33. 344	15. 286	74. 024	1. 00 44. 10
	ATOM	3409	CA	ARG	447	34. 615	15. 878	73. 615	1. 00 44. 23
20	MOTA	3410	CB	ARG	447	35. 765	15. 244	74. 396	1. 00 44. 71
	ATOM	3411	CG	ARG	447	36. 079	15. 917	75. 720	1. 00 46. 63
	ATOM	3412	CD	ARG	447	36. 405	14. 896	76. 794	1. 00 48. 87
•	ATOM	3413	NE	ARG	447	37. 226	13. 804	76. 286	1. 00 53. 97
	ATOM	3414	CZ	ARG	447	38. 507	13. 915	75. 956	1. 00 55. 65
25	ATOM	3415	NH1	ARG	447	39. 130	15. 076	76. 085	1. 00 56. 71
	ATOM	3416	NH2	ARG	447	39. 161	12. 862	75. 486	1. 00 58. 00
	ATOM	3417	С	ARG	447	34. 891	15. 739	72. 122	1. 00 45. 53
	ATOM	3418	0	ARG	447	35. 506	16. 617	71. 508	1. 00 45. 95
	ATOM	3419	N	GLY	448	34. 444	14. 630	71. 543	1. 00 45. 12

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	ATOM	3420	CA	GLY	448	34. 667		70. 129	1. 00	43. 75
	ATOM	3421	C	GLY	448	33. 915		69. 275		44. 42
	ATOM	3422	0	GLY	448	34. 497		68. 401		43. 25
	ATOM	3423	N	ALA	449	32. 617	15. 508	69. 530		44. 33
5	ATOM	3424	CA	ALA	449	31. 764	16. 435	68. 798	1. 00	46. 02
	ATOM	3425	СВ	ALA	449	30. 349		69. 362	1. 00	44. 02
	ATOM	3426	C	ALA	449	32. 334	17. 852	68. 901		47. 27
	ATOM	3427	0	ALA	449	32. 388	8 18. 585	67. 910	1. 00	46. 99
	ATOM	3428	N	ALA	450	32. 771	18. 226	70. 100	1. 00	47. 32
10	ATOM	3429	CA	ALA	450	33. 337	19. 549	70. 320	1. 00	48. 93
	ATOM	3430	СВ	ALA	450	33. 590	19. 771	71. 803	1. 00	48. 70
	ATOM	3431	С	ALA	450	34. 630	19. 752	69. 537	1. 00	49. 10
	ATOM	3432	0	ALA	450	34. 795	20. 770	68. 864	1. 00	51. 55
	ATOM	3433	N	LEU	451	35. 546	18. 792	69. 625	1. 00	47. 13
15	ATOM	3434	CA	LEU	451	36. 828	18. 889	68. 923	1. 00	46. 08
	ATOM	3435	CB	LEU	451	37. 693	17. 661	69. 226	1. 00	43. 72
	ATOM	3436	CG	LEU	451	38. 376	17. 636	70. 598	1. 00	44. 07
	ATOM	3437	CD1	LEU	451	38. 798	16. 218	70. 955	1. 00	41. 74
	ATOM	3438	CD2	LEU	451	39. 577	18. 574	70. 574	1. 00	40. 23
20	ATOM	3439	C	LEU	451	36. 672	19. 055	67. 410	1. 00	45. 46
	ATOM	3440	0	LEU	451	37. 495	19. 708	66. 760	1. 00	46. 36
	ATOM	3441	N	VAL	452	35. 618	18. 465	66. 857	1. 00	43. 95
	ATOM	3442	CA	VAL	452	35. 348	18. 552	65. 428	1. 00	44. 38
	ATOM	3443	CB	VAL	452	34. 426	17. 376	64. 959	1. 00	43. 85
25	ATOM	3444	CG1	VAL	452	33. 998	17. 576	63. 513	1. 00	41. 59
	ATOM	3445	CG2	VAL	452	35. 169	16. 040	65. 087	1. 00	40. 86
	ATOM	3446	C	VAL	452	34. 687	19. 905	65. 125	1. 00	45. 31
	ATOM	3447	0	VAL	452	34. 881	20. 482	64. 056	1. 00	42. 97
	ATOM	3448	N	SER	453	33. 912	20. 411	66. 077	1. 00	46. 60

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	ATOM	3449	CA	SER	453	33. 253	21. 693	65. 900	1. 00 49. 07
	ATOM	3450	CB	SER	453	32. 204	21. 902	66. 986	1. 00 47. 21
	ATOM	3451	0G	SER	453	31. 146	20. 972	66. 845	1. 00 44. 37
	ATOM	3452	C	SER	453	34. 293	22. 806	65. 951	1. 00 51. 53
5	ATOM	3453	0	SER	453	34. 150	23. 820	65. 281	1. 00 52. 56
	ATOM	3454	N	ALA	454	35. 352	22. 593	66. 728	1. 00 54. 40
	MOTA	3455	CA	ALA	454	36. 430	23. 567	66. 881	1. 00 56. 39
	ATOM	3456	CB	ALA	454	37. 336	23. 158	68. 031	1. 00 55. 74
	ATOM	3457	C	ALA	454	37. 259	23. 751	65. 614	1. 00 58. 75
10	ATOM	3458	0	ALA	454	37. 863	24. 807	65. 408	1. 00 59. 45
	ATOM	3459	N	VAL	455	37. 310	22. 719	64. 779	1. 00 60. 29
	ATOM	3460	CA	VAL	455	38. 063	22. 796	63. 535	1. 00 61. 78
	ATOM	3461	CB	VAL	455	38. 603	21. 416	63. 112	1. 00 61. 44
	ATOM	3462	CG1	VAL	455	39. 090	21. 464	61. 672	1. 00 60. 81
15	ATOM	3463	CG2	VAL	455	39. 737	21. 005	64. 031	1. 00 60. 68
	ATOM	3464	C	VAL	455	37. 152	23. 330	62. 442	1. 00 63. 56
	ATOM	3465	0	VAL	455	37. 550	24. 176	61. 643	1. 00 63. 25
	ATOM	3466	N	ALA	456 ~	35. 921	22. 835	62. 416	1. 00 65. 38
	ATOM	3467	CA	ALA	456	34. 959	23. 275	61. 422	1. 00 69. 39
20	ATOM	3468	CB	ALA	456	33. 751	22. 354	61. 423	1. 00 68. 17
	ATOM	3469	C	ALA	456	34. 522	24. 709	61.710	1. 00 73. 10
	ATOM	3470	0	ALA	456	33. 975	25. 382	60. 837	1. 00 73. 04
	ATOM	3471	N	CYS	457	34. 771	25. 170	62. 935	1. 00 77. 06
	ATOM	3472	CA	CYS	457	34. 390	26. 521	63. 341	1. 00 81. 01
25	ATOM	3473	CB	CYS	457	34. 192	26. 599	64. 856	1. 00 80. 51
	ATOM	3474	SG	CYS	457	33. 478	28. 151	65. 432	1. 00 81. 75
	ATOM	3475	C	CYS	457	35. 420	27. 554	62. 916	1. 00 83. 65
	ATOM	3476	0	CYS	457	35. 312	28. 726	63. 275	1. 00 85. 11
	ATOM	3477	N	LYS	458	36. 430	27. 118	62. 172	1. 00 86. 29

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	ATOM	3478	CA	LYS	458	37. 441	28. 041	61. 683	1. 00 89. 14
	ATOM	3479	CB	LYS	458	38. 843	27. 441	61. 803	1. 00 88. 60
	ATOM	3480	CĢ	LYS	458	39. 932	28. 486	61. 632	1. 00 89. 51
	ATOM	3481	CD	LYS	458	41. 276	27. 992	62. 130	1. 00 89. 70
5	ATOM	3482	CE	LYS	458	42. 257	29. 146	62. 269	1. 00 89. 22
	ATOM	3483	NZ	LYS	458	41. 718	30. 194	63. 180	1. 00 88. 81
	ATOM	3484	C	LYS	458	37. 096	28. 310	60. 232	1. 00 91. 26
	ATOM	3485	0	LYS	458	37. 936	28. 733	59. 438	1. 00 91. 56
	ATOM	3486	N	LYS	459	35. 834	28. 043	59. 901	1. 00 93. 94
10	ATOM	3487	CA	LYS	459	35. 302	28. 240	58. 548	1. 00 96. 28
	ATOM	3488	CB	LYS	459	35. 323	26. 923	57. 765	1. 00 96. 25
	ATOM	3489	CG	LYS	459	36. 719	26. 409	57. 421	1. 00 96. 30
	ATOM	3490	CD	LYS	459	37. 458	27. 348	56. 475	1. 00 96. 73
	ATOM	3491	CE	LYS	459	38. 833	26. 801	56. 111	1. 00 97. 12
15	ATOM	3492	NZ	LYS	459	39. 577	27. 717	55. 197	1. 00 97. 75
	ATOM	3493	C	LYS	459	33. 863	28. 759	58. 624	1. 00 97. 78
	ATOM	3494	0	LYS	459	33. 417	29. 516	57. 758	1. 00 98. 11
	ATOM	3495	N	ALA	460	33. 153	28. 327	59. 666	1. 00 99. 29
	ATOM	3496	CA	ALA	460	31. 778	28. 738	59. 916	1. 00100. 54
20	ATOM	3497	CB	ALA	460	31. 028	27. 644	60. 681	1. 00100. 58
	ATOM	3498	C	ALA	460	31. 765	30. 042	60. 719	1. 00101. 56
	ATOM	3499	0	ALA	460	30. 755	30. 750	60. 777	1. 00101. 79
	ATOM	3500	N	CYS	461	32. 899	30. 360	61. 338	1. 00102. 59
	ATOM	3501	CA	CYS	461	33. 033	31. 572	62. 156	1. 00103. 00
25	ATOM	3502	CB	CYS	461	33. 145	31. 169	63. 624	1. 00103. 05
	ATOM	3503	SG	CYS	461	33. 354	32. 536	64. 774	1. 00103. 32
	ATOM	3504	C	CYS	461	34. 265	32. 367	61. 753	1. 00103. 21
	ATOM	3505	0	CYS	461	34. 788	33. 098	62. 620	1. 00103. 54
	ATOM	3506	OXT	CYS	461	34. 665	32. 248	60. 578	1. 00103. 24

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	TER 3507		YS 461							
	ATOM	3508	C1	GLC	500	23. 469	1. 767	65. 521	1. 00	30. 82
	ATOM	3509	C2	GLC	500	23. 418	3. 122	64. 706	1. 00	29. 40
	MOTA	3510	C3	GLC	500	24. 837	3. 619	64. 445	1. 00	29. 78
5	ATOM	3511	C4	GLC	500	25. 496	3. 860	65. 778	1. 00	28. 77
	ATOM	3512	C5	GLC	500	25. 529	2. 514	66. 593	1. 00	27. 72
	ATOM	3513	C6	GLC	500	26. 162	2. 717	67. 936	1. 00	26. 98
	ATOM	3514	01	GLC	500	24. 127	0. 765	64. 857	1. 00	36. 62
	ATOM	3515	02	GLC	500	22. 756	2. 872	63. 483	1. 00	32. 75
10	ATOM	3516	03	GLC	500	24. 786	4. 837	63. 698	1. 00	29. 31
	ATOM	3517	04	GLC	500	26. 853	4. 253	65. 639	1. 00	29. 10
	ATOM	3518	05	GLC	500	24. 152	2. 040	66. 770	1. 00	29. 59
	ATOM	3519	06	GLC	500	25. 517	3. 687	68. 814	1. 00	30. 98
	TER 35	20 G	LC	500						
15	ATOM	3521	S 1	CP1	501	36. 312	19. 051	60. 824	1. 00	50. 83
	ATOM	3522	C2	CP1	501	35. 720	19. 405	59. 240	1. 00	49. 96
	ATOM	3523	C3	CP1	501	36. 398	18. 662	58. 318	1. 00	49. 96
	ATOM	3524	N4	CP1	501	37. 363	17. 829	58. 827	1. 00	49. 99
	ATOM	3525	C5	CP1	501	37. 429	17. 932	60. 162	1. 00	49. 39
20	ATOM	3526	N6	CP1	501	38. 317	17. 183	60. 878	1. 00	48. 07
	ATOM	3527	C7	CP1	501	38. 575	17. 220	62. 294	1. 00	46. 71
	ATOM	3528	80	CP1	501	37. 968	18. 001	63. 039	1. 00	47. 48
	ATOM	3529	C9	CP1	501	40. 386	16. 405	64. 107	1. 00	46. 71
	ATOM	3530	C10	CP1	501	39. 620	16. 253	62. 884	1. 00	47. 34
25	ATOM	3531	C11	CP1	501	39. 831	15. 053	62. 110	1. 00	46. 39
	ATOM	3532	C12	CP1	501	40. 749	14. 066	62. 520	1. 00	46. 34
	ATOM	3533	C13	CP1	501	41. 496	14. 237	63. 722	1. 00	47. 57
	ATOM	3534	F	CP1	501	42. 392	13. 310	64. 155	1. 00	48. 24
	ATOM	3535	C15	CP1	501	41. 306	15. 404	64. 502	1. 00	46. 98

- 138 -**ATOM** 3536 S16 CP1 501 40. 907 12. 638 61. 485 1.00 44.61 ATOM 3537 N17 CP1 501 42. 782 10.864 62. 327 1. 00 40. 11 ATOM 3538 C18 CP1 501 42. 525 11. 942 61. 488 1. 00 41. 49 ATOM 3539 N19 CP1 501 43. 528 12. 436 60.686 1. 00 42. 95 5 ATOM 3540 C20 CP1 501 44. 549 11. 571 61.054 1.00 43.00 ATOM 3541 C21 CP1 501 44. 116 10. 651 62. 014 1. 00 39. 24 ATOM 3542 C22 CP1 501 41. 894 10. 152 63. 276 1. 00 32. 83 ATOM 3543 N23 CP1 501 40. 279 17. 465 64. 913 1. 00 46. 10 TER 3544 CP1 501 JJJJ 3545 NA+1 NA1 ATOM 10 600 36. 903 10. 609 46. 484 1.00 48.71 **ATOM** 3546 0 HOH 601 20. 332 -23. 624 70. 208 1.00 45.57 ATOM 3547 0 HOH 602 18. 766 -22. 456 65. 630 1. 00 41. 87 **ATOM** 3548 0 HOH 603 13. 471 -20. 599 70. 297 1. 00 45. 83 ATOM 3549 0 HOH 604 11. 104 -30. 408 72. 307 1. 00 48. 61 ATOM 3550 0 15 HOH 605 6. 606 -26. 352 79. 319 1. 00 59. 47 ATOM 3551 0 HOH 606 15. 315 -28. 400 85. 522 1. 00 48. 85 **ATOM** 3552 0 HOH 607 18. 765 -29. 705 82. 807 1. 00 55. 60 ATOM 3553 0 HOH 608 27. 649 -22. 465 84. 914 1. 00 39. 29 ATOM 3554 0 HOH 609 28. 890 -18. 936 88. 942 1.00 38.24 **ATOM** 20 3555 0 HOH 610 31. 397 -19. 437 88. 300 1. 00 44. 33 ATOM 3556 0 HOH 611 33. 495 -12. 487 88. 943 1. 00 40. 63 ATOM 3557 0 HOH 612 28. 110 -14. 193 93. 119 1. 00 37. 41 ATOM 3558 0 HOH 613 22. 501 -9. 921 93. 883 1. 00 55. 62 **ATOM** 3559 0 HOH 614 18. 084 -9. 259 91. 966 1. 00 48. 69 25 ATOM 3560 0 HOH 615 19. 985 -7. 585 89. 518 1. 00 54. 30 ATOM 3561 0 HOH 616 18. 162 -4. 982 77. 583 1. 00 42. 44 ATOM 3562 0 HOH 617 15. 728 -5. 792 77. 752 1.00 49.61 ATOM 3563 0 HOH 618 17. 869 -7. 338 75. 263 1. 00 52. 43 ATOM 3564 0 HOH 619 14. 631 -9. 827 77. 339 1. 00 27. 38

- 139 -ATOM 3565 0 HOH 620 14. 305 -5. 926 69. 446 1. 00 38. 14 **ATOM** 3566 HOH 0 621 13. 616 -3.08768. 452 1. 00 51. 29 ATOM 3567 HOH 622 66.865 0 15. 537 -2.6021. 00 35. 42 3568 ATOM 0 HOH 623 18. 821 -1.83165. 405 1. 00 31. 67 ATOM 3569 5 0 HOH 624 17. 261 0. 174 60. 996 1. 00 34. 87 ATOM 3570 0 HOH 625 18. 895 -0.65358. 995 1. 00 41. 82 ATOM 3571 0 HOH 626 20. 053 -2.47855. 373 1. 00 35. 91 ATOM 3572 0 HOH 55.062 627 22. 217 -1.0191. 00 36. 64 ATOM 3573 0 HOH 56. 470 628 25. 137 -0.1531. 00 24. 69 **ATOM** 3574 59.774 0 HOH 629 22.562 1.498 1. 00 31. 68 10 **ATOM** 3575 HOH 630 24.912 0.122 62. 135 1. 00 25. 12 0 ATOM 3576 0 HOH 631 25. 071 71. 129 1. 00 26. 49 2. 179 **ATOM** 3577 HOH 27. 157 71. 903 0 632 5.888 1. 00 41. 05 **ATOM** 3578 0 HOH 633 29. 481 7. 227 73. 290 1. 00 47. 52 ATOM 3579 0 HOH 634 31. 223 8.383 71. 417 15 1. 00 44. 33 3580 ATOM 0 HOH 635 32. 517 7. 788 77. 983 1. 00 44. 30 ATOM 3581 0 HOH 636 35. 945 15. 748 80. 298 1. 00 32. 85 ATOM 3582 0 HOH 41.395 74. 250 637 13. 522 1. 00 52. 40 **ATOM** 3583 0 HOH 638 41. 454 16.603 73. 492 1. 00 35. 38 ATOM 3584 44. 238 20 0 HOH 639 18.657 64. 621 1. 00 57. 41 **ATOM** 3585 0 HOH 48. 524 12.679 62.857 640 1. 00 55. 80 **ATOM** 3586 0 HOH 50.088 10.035 69.707 641 1. 00 37. 86 ATOM 3587 0 HOH 642 47.834 4.897 73.654 1. 00 43. 91 **ATOM** 3588 0 HOH 643 47. 658 2.456 75. 515 1. 00 46. 89 ATOM 3589 HOH 45.862 75. 793 25 0 644 0.872 1. 00 36. 22 **ATOM** 3590 0 HOH 42. 167 -0.40177. 407 645 1. 00 46. 09 ATOM 3591 HOH 39. 939 76. 818 0 646 -1.6641. 00 28. 80

41.804

35. 946

2. 590

-0. 230 81. 704

77. 672

1. 00 30. 06

1. 00 44. 47

ATOM

ATOM

3592

3593

0

0

HOH

HOH

647

648

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	ATOM	3594	0	НОН	649	35. 692 -3. 832	84. 533	1. 00 48. 68
	MOTA	3595	0	НОН	650	35. 503 -5. 648	82. 602	1. 00 39. 36
	ATOM	3596	0	НОН	651	34. 249 -6. 282	78. 743	1. 00 28. 80
	ATOM	3597	0	НОН	652	41. 570 -6. 014	79. 114	1. 00 41. 31
5	ATOM	3598	0	НОН	653	42. 725 -8. 259	76. 851	1. 00 34. 12
	ATOM	3599	0	НОН	654	42. 400 -10. 619	75. 649	1. 00 32. 12
	ATOM	3600	0	НОН	655	44. 745 -10. 112	73. 414	1. 00 30. 95
	ATOM	3601	0	НОН	656	44. 977 -6. 287	75. 709	1. 00 54. 82
	ATOM	3602	0	НОН	657	49. 536 -3. 896	71. 639	1. 00 46. 68
10	ATOM	3603	0	НОН	658	47. 500 -6. 424	68. 659	1. 00 37. 00
	ATOM	3604	0	НОН	659	46. 887 -8. 289	65. 948	1. 00 35. 73
	ATOM	3605	0	НОН	660	45. 007 -14. 004	70. 403	1. 00 31. 53
	ATOM	3606	0	НОН	661	44. 785 -16. 666	70. 958	1. 00 39. 67
	ATOM	3607	0	НОН	662	39. 546 -15. 899	74. 666	1. 00 38. 86
15	ATOM	3608	0	НОН	663	38. 539 -14. 985	72. 232	1. 00 34. 80
	ATOM	3609	0	НОН	664	38. 252 -17. 032	68. 208	1. 00 47. 76
	ATOM	3610	0	НОН	665	39. 836 -15. 454	66. 437	1. 00 38. 55
	ATOM	3611	0	НОН	666	36. 975 -19. 549	67. 636	1. 00 43. 12
	ATOM	3612	0	НОН	667	37. 200 -20. 262	70. 388	1. 00 51. 64
20	ATOM	3613	0	НОН	668	33. 328 -20. 695	70. 543	1. 00 49. 91
	ATOM	3614	0	НОН	669	32. 877 -18. 716	69. 209	1. 00 30. 69
	ATOM	3615	0	НОН	670	30. 463 -18. 228	69. 770	1. 00 29. 35
	ATOM	3616	0	НОН	671	29. 403 -18. 862	72. 028	1. 00 29. 94
	ATOM	3617	0	НОН	672	31. 677 -19. 876	75. 929	1. 00 57. 83
25	ATOM	3618	0	НОН	673	32. 105 -15. 120	81. 811	1. 00 56. 36
	ATOM	3619	0	НОН	674	25. 408 -13. 262	70. 399	1. 00 19. 73
	ATOM	3620	0	НОН	675	20. 199 -11. 770	66. 567	1. 00 31. 95
	ATOM	3621	0	НОН	676	20. 589 -11. 169	63. 684	1. 00 28. 18
	ATOM	3622	0	НОН	677	18. 416 -12. 169	62. 695	1. 00 34. 73

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	ATOM	3623	0	НОН	678	18. 037 -	12. 657	56. 097	1. 00 62. 31
	ATOM	3624	0	НОН	679	15. 700 -1	10. 616	55. 942	1. 00 49. 61
	ATOM	3625	0	НОН	680	17. 485 -	-8. 240	55. 372	1. 00 37. 91
	ATOM	3626	0	НОН	681	22. 370 -1	2. 555	56. 733	1. 00 27. 53
5	ATOM	3627	0	НОН	682	21. 048 -1	6. 039	51. 265	1. 00 53. 09
	ATOM	3628	0	НОН	683	25. 649 -	8. 890	49. 620	1. 00 43. 30
	ATOM	3629	0	НОН	684	25. 472 -	5. 908	50. 031	1. 00 43. 23
	ATOM	3630	0	НОН	685	27. 841 -	3. 633	51. 119	1. 00 34. 64
	ATOM	3631	0	НОН	686	23. 209	1. 359	50. 792	1. 00 44. 06
10	ATOM	3632	0	НОН	687	26. 198	3. 711	50. 151	1. 00 38. 65
	ATOM	3633	0	НОН	688	27. 728	6. 416	50. 494	1. 00 39. 66
	ATOM	3634	0	НОН	689	30. 171	5. 238	50. 152	1. 00 36. 90
	ATOM	3635	0	НОН	690	32. 248	6. 334	48. 750	1. 00 33. 36
	ATOM	3636	0	НОН	691	36. 665	2. 495	46. 196	1. 00 32. 68
15	ATOM	3637	0	НОН	692	37. 821	0. 573	47. 634	1. 00 47. 42
	ATOM	3638	0	НОН	693	42. 794	0. 201	52. 097	1. 00 44. 65
	ATOM	3639	0	НОН	694	41. 559	1. 725	53. 810	1. 00 38. 52
	ATOM	3640	0	НОН	695	43. 105	3. 662	55. 242	1. 00 34. 89
	ATOM	3641	0	НОН	696	45. 510	2. 836	56. 086	1. 00 40. 92
20	ATOM	3642	0	НОН	697	50. 206	2. 510	60. 598	1. 00 45. 86
	ATOM	3643	0	НОН	698	52. 258	1. 308	61. 720	1. 00 45. 43
	ATOM	3644	0	НОН	699	48. 954	1. 961	67. 618	1. 00 35. 43
	ATOM	3645	0	НОН	700	49. 694 -(). 399	68. 442	1. 00 39. 38
	ATOM	3646	0	НОН	701	40.015 -5	5. 106	51. 960	1. 00 36. 49
25	ATOM	3647	0	НОН	702	34. 048 -12	2. 903	50. 839	1. 00 37. 87
	ATOM	3648	0	НОН	703	33. 190 -14	1. 541	52. 882	1. 00 51. 09
	ATOM	3649	0	НОН	704	34. 961 -16	. 254	52. 067	1. 00 35. 42
	ATOM	3650	0	НОН	705	30. 397 -15	. 105	52. 902	1. 00 39. 69
	ATOM	3651	0	НОН	706	31.770 -20	. 985	57. 467	1. 00 48. 16

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ATOM 3652 0 HOH 707 37. 192 -19. 637 55. 866 1.00 46.43 ATOM 3653 0 HOH 708 38. 187 -23. 567 61. 924 1.00 40.92 ATOM 3654 0 HOH 709 38. 470 -23. 126 65. 456 1. 00 45. 43 ATOM 3655 0 HOH 710 30. 533 -23. 844 62. 578 1. 00 37. 90 ATOM 5 3656 0 HOH 711 26. 515 -21. 678 62. 544 1.00 39.08 **ATOM** 3657 0 HOH 712 27. 242 -20. 400 65. 671 1.00 33.60 **ATOM** 3658 0 HOH 713 25. 907 -18. 116 65. 171 1.00 24.64 ATOM 3659 0 HOH 714 28. 226 -26. 567 74. 622 1. 00 44. 93 ATOM 3660 O HOH 715 31. 091 -28. 151 73. 632 1.00 39.43 10 ATOM 3661 0 HOH 716 28. 020 -32. 685 74. 512 1. 00 48. 35 **ATOM** 3662 0 HOH 717 28. 401 -36. 363 77. 956 1. 00 47. 24 ATOM 3663 0 HOH 718 26. 796 -22. 733 95. 375 1. 00 34. 50 ATOM 3664 0 HOH 719 23. 506 -18. 729 96. 532 1. 00 46. 50 ATOM 3665 0 HOH 720 7. 193 -13. 392 87. 134 1.00 48.33 15 **ATOM** 3666 0 HOH 721 23. 769 -2. 393 77. 130 1. 00 39. 79 ATOM 3667 0 HOH 722 21. 538 6. 141 76. 432 1. 00 52. 58 ATOM 3668 0 HOH 26.038 723 13. 552 80. 579 1. 00 47. 60 ATOM 3669 0 HOH 72425. 460 9. 823 62. 329 1. 00 33. 10 **ATOM** 3670 0 HOH 725 27. 321 10. 443 60. 403 1. 00 39. 23 20 ATOM 3671 0 HOH 726 26. 658 8.602 58.871 1. 00 32. 16 ATOM 3672 0 HOH 727 29.670 11.059 61.417 1. 00 24. 95 ATOM 3673 0 HOH 728 30. 585 13. 937 60. 932 1. 00 41. 90 **ATOM** 3674 0 HOH 729 34. 591 18. 790 55.094 1.00 40.47 ATOM 3675 0 HOH 730 34. 117 19. 353 52. 182 1. 00 54. 62 ATOM 25 3676 0 HOH 731 31. 428 16.535 48. 224 1. 00 37. 06 **ATOM** 3677 0 HOH 732 31. 432 15. 488 46. 047 1. 00 33. 85 ATOM 3678 0 HOH 733 27.660 11. 291 51. 289 1. 00 40. 74 **ATOM** 3679 0 HOH 734 27. 629 10.029 53. 857 1. 00 30. 56 ATOM 3680 O HOH 735 22.996 7. 311 45. 724 1.00 57.65

					- 1	43 -			
ATOM	3681	0	НОН	736	25. 532	2. 038	43. 263	1. 00	34. 43
ATOM	3682	0	НОН	737	33. 508	3. 221	40. 211	1. 00	45. 05
ATOM	3683	0	НОН	738	35. 525	1. 426	41. 242	1. 00	44. 71
ATOM	3684	0	НОН	739	37. 227	9. 576	44. 352	1. 00	31. 96
ATOM	3685	0	НОН	740	39. 858	15. 804	52. 237	1. 00	43. 41
ATOM	3686	0	НОН	741	42. 053	15. 415	53. 940	1. 00	47. 39
ATOM	3687	0	НОН	742	32. 200	24. 148	58. 683	1. 00	45. 42
ATOM	3688	0	НОН	743	28. 016	21. 804	51. 201	1. 00	44. 12
ATOM	3689	0	НОН	744	22. 797	26. 498	63. 763	1. 00	53. 69
ATOM	3690	0	НОН	745	10. 552	26. 073	62. 119	1. 00	43. 13
ATOM	3691	0	НОН	746	11. 190	7. 673	68. 338	1. 00	57. 06
ATOM	3692	0	НОН	747	20. 818	-3. 881	51. 225	1. 00	56. 55
ATOM	3693	0	НОН	748	29. 885	-6. 633	43. 981	1. 00	46. 17

5

10

15

TER

3695

HOH

なお、表1は、当業者によって慣用されているプロテイン・データ・バンク の表記方法に準拠して作成されている。表1中、GLCはグルコース分子を表 し、CP1は式III a で表される化合物を表し、HOHは水分子を表す。

ATOM 3694 0 HOH 749 40.811 30.945 68.309 1.00 45.88

また、本発明においては、配列番号8に示すGKタンパク質の結晶を調製することに成功している(後述の実施例参照)。そしてこのようにして得られたGKタンパク質の結晶は、格子定数が、下記式(5)~(8):

25 $a=b=103. 2\pm 5$ オングストローム … (5) $c=281. 0\pm 7$ オングストローム … (6) $\alpha=\beta=90^\circ$ … (7) $\gamma=120^\circ$ … (8)

を満たすものであった。また、この結晶は、空間群が $P6_522$ であることが

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解明された。ここで、前記 a=b は 103.2 ± 3 オングストロームであることが好ましく、 103.2 ± 2 オングストロームであることがより好ましく、 103.2 ± 1 オングストロームであることがさらに好ましい。また、前記 c は 281.0 ± 6 オングストロームであることが好ましく、 281.0 ± 4 オングストロームであることがより好ましく、 281.0 ± 4 オングストロームであることがより好ましく、 281.0 ± 2 オングストロームであることがさらに好ましい。このようにして得られたGKタンパク質結晶の3次元構造座標を表2に示す。

	表 2								
	ATOM	1	CB	MET	15	54. 150	5. 972	67. 103	1. 00 55. 10
10	ATOM	2	CG	MET	15	55. 594	5. 943	67. 591	1. 00 55. 46
	ATOM	3	SD	MET	15	56. 013	4. 505	68. 603	1. 00 52. 92
	ATOM	4	CE	MET	15	56. 517	5. 326	70. 108	1. 00 51. 73
	ATOM	5	C	MET	15	52. 357	4. 955	65. 669	1. 00 56. 87
	ATOM	6	0	MET	15	52. 057	4. 609	64. 524	1. 00 57. 60
15	ATOM	7	N	MET	15	54. 770	4. 766	65. 028	1. 00 55. 00
	ATOM	8	CA	MET	15	53. 800	4. 813	66. 167	1. 00 56. 04
	ATOM	9	N	VAL	16	51. 468	5. 456	66. 525	1. 00 55. 58
	ATOM	10	CA	VAL	16	50. 065	5. 625	66. 154	1. 00 52. 87
	ATOM	11	CB	VAL	16	49. 141	4. 862	67. 129	1. 00 49. 32
20	ATOM	12	CG1	VAL	16	47. 696	5. 016	66. 716	1. 00 48. 26
	ATOM	13	CG2	VAL	16	49. 508	3. 394	67. 126	1. 00 47. 28
	ATOM	14	C	VAL	16	49. 666	7. 097	66. 085	1. 00 53. 26
	ATOM	15	0	VAL	16	49. 218	7. 563	65. 040	1. 00 52. 32
	ATOM	16	N	GLU	17	49. 845	7. 828	67. 182	1. 00 56. 12
25	ATOM	17	CA	GLU	17	49. 511	9. 253	67. 210	1. 00 59. 41
	ATOM	18	CB	GLU	17	50. 102	9. 921	68. 456	1. 00 63. 35
	ATOM	19	CG	GLU	17	49. 063	10. 373	69. 484	1. 00 68. 69
	ATOM	20	CD	GLU	17	48. 174	11. 525	69. 004	1. 00 72. 00
	ATOM	21	0E1	GLU	17	47. 314	11. 964	69. 805	1. 00 74. 22

- 145 -ATOM 22 0E2 GLU 17 48. 328 11. 992 67. 847 1. 00 72. 36 ATOM 23 C **GLU 17** 50.035 9. 963 65. 967 1. 00 59. 05 ATOM 240 GLU 17 49. 521 11. 011 65. 566 1. 00 57. 70 ATOM 25 N **GLN 18** 51.070 9. 389 65. 367 1.00 60.75 **ATOM** 5 26 CA **GLN** 18 51.661 64. 170 9.960 1. 00 61. 70 ATOM 27 CB **GLN 18** 53. 038 9. 329 63.895 1.00 66.55 ATOM 28 CG GLN 18 54.001 9. 219 65. 110 1. 00 72. 22 ATOM 29 CD **GLN** 18 54. 509 10. 566 65. 654 1. 00 75. 87 ATOM 30 OE1 GLN 18 55. 317 10.605 66. 595 1. 00 75. 55 10 **ATOM** 31 NE2 GLN 18 54. 037 11.669 65.067 1. 00 77. 63 C ATOM 32**GLN** 18 50.709 9.682 63.004 1. 00 59. 33 33 0 ATOM **GLN** 18 50. 322 62. 287 10.601 1. 00 59. 09 ATOM 34 N **ILE 19** 50. 321 8. 418 62. 832 1. 00 55. 64 **ATOM** 35 CA ILE 19 49. 416 61.747 8. 029 1. 00 53. 41 15 ATOM 36 CB ILE 19 49. 113 6. 529 61.778 1.00 52.34 ATOM CG2 ILE 19 37 47. 964 60. 832 6. 211 1. 00 50. 69 ATOM CG1 ILE 19 38 50. 374 61.389 5. 754 1. 00 52. 73 **ATOM** 39 CD1 ILE 19 50. 186 4. 256 61. 274 1. 00 53. 73 ATOM 40 C ILE 19 48. 088 8. 774 61.741 1. 00 53. 03 20 ATOM 41 0 ILE 19 47. 791 60. 812 9. 528 1. 00 52. 86 ATOM 42 N LEU 20 47. 279 8. 548 62. 766 1. 00 52. 38 ATOM 43 CA LEU 20 45.997 9. 228 62.861 1. 00 51. 95 ATOM 44 CBLEU 20 45. 336 8. 937 64. 195 1. 00 50. 70 ATOM 45 CG LEU 20 44. 563 7. 632 64. 212 1. 00 51. 65 ATOM CD1 LEU 20 25 46 45. 450 63.803 6. 454 1. 00 51. 77 ATOM CD2 LEU 20 47 44.010 65. 599 1. 00 51. 02 7. 463 ATOM 48 C LEU 20 46. 158 10.723 62. 727 1. 00 52. 33 ATOM 49 0 LEU 20 45. 204 11. 427 62. 401 1. 00 54. 11

ATOM

50 N

ALA 21

47. 366

11. 207

62. 990

1. 00 51. 49

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	ATOM	51	CA	ALA	21	47.	643	12. 628	62. 907	1. 00	49. 87
	ATOM	52	CB	ALA	21	49. (066	12. 899	63. 342	1. 00	50. 58
	ATOM	53	C	ALA	21	47.	414	13. 133	61. 491	1. 00	48. 63
	ATOM	54	0	ALA	21	47. (090	14. 301	61. 286	1. 00	47. 74
5	ATOM	55	N	GLU	22	47. 5	571	12. 243	60. 517	1. 00	47. 60
	ATOM	56	CA	GLU	22	47. 3	383	12. 605	59. 121	1. 00	48. 69
	ATOM	57	CB	GLU	22	47. 8	818	11. 457	58. 215	1. 00	51. 49
	ATOM	58	CG	GLU	22	49. 2	282	11. 520	57. 838	1. 00	59. 47
	ATOM	59	CD	GLU	22	49. 7	738	10. 335	57. 003	1. 00	64. 78
10	ATOM	60	0E1	GLU	22	50. 8	896	10. 369	56. 519	1. 00	66. 47
	ATOM	61	0E2	GLU	22	48. 9	948	9. 373	56. 839	1. 00	68. 05
	ATOM	62	C	GLU	22	45. 9	954	12. 999	58. 794	1. 00	48. 26
	ATOM	63	0	GLU	22	45. 6	383	13. 538	57. 721	1. 00	48. 86
	ATOM	64	N	PHE	23	45. 0)36	12. 733	59. 715	1. 00	47. 14
15	ATOM	65	CA	PHE	23	43. 6	641	13. 076	59. 490	1. 00	45. 51
	ATOM	66	CB	PHE	23	42. 7	722	12. 045	60. 147	1. 00	41. 36
	ATOM	67	CG	PHE.	23	42. 5	544	10. 783	59. 347	1. 00	37. 96
	ATOM	68	CD1	PHE	23	43. 2	808	9. 613	59. 697	1. 00	35. 23
	ATOM	69	CD2	PHE	23	41. 6	887	10. 758	58. 255	1. 00	37. 67
20	ATOM	70	CE1	PHE	23	43. 0	16	8. 435	58. 968	1. 00	32. 67
	ATOM	71	CE2	PHE	23	41. 4	192	9. 583	57. 523	1. 00	37. 15
	ATOM	72	CZ	PHE	23	42. 1	.58	8. 423	57. 883	1. 00	33. 48
	ATOM	73	C	PHE	23	43. 3	10	14. 468	60. 013	1. 00	47. 24
	ATOM	74	0	PHE	23	42. 2	27	14. 993	59. 767	1. 00	46. 34
25	ATOM	75	N	GLN	24	44. 2	45	15. 068	60. 735	1. 00	50. 44
	ATOM	76	CA	GLN	24	44. 0	28 1	16. 400	61. 279	1. 00	55. 06
	ATOM	77	CB	GLN	24	45. 3	06 1	16. 882	61. 979	1. 00	59. 10
	ATOM	78	CG	GLN	24	45. 7	15 1	6. 023	63. 168	1. 00	62. 03
	ATOM	79	CD	GLN	24	44. 6	86 1	6. 075	64. 277	1. 00	65. 56

- 147 -ATOM 80 0E1 GLN 24 44. 653 15. 207 65. 156 1. 00 66. 95 ATOM NE2 GLN 24 81 43. 834 17. 103 64. 245 1. 00 65. 89 ATOM 82 C **GLN 24** 43. 644 17. 359 60. 149 1.00 56.09 ATOM 83 0 GLN 24 43.892 17.073 58.979 1.00 57.63 ATOM N 5 84 LEU 25 43.016 18. 476 60.504 1. 00 55. 99 ATOM CA LEU 25 85 42.616 19. 501 59.540 1. 00 55. 27 ATOM 86 CB LEU 25 41. 303 19. 128 58. 841 1.00 54.71 ATOM CG LEU 25 87 41. 325 17. 896 57. 922 1.00 53.30 ATOM 88 CD1 LEU 25 39. 928 17. 618 57. 419 1. 00 53. 18 ATOM CD2 LEU 25 10 89 42. 264 18. 113 56. 755 1.00 51.55 ATOM 90 C LEU 25 42. 444 20. 786 60. 336 1.00 56.31 **ATOM** LEU 25 91 0 41. 377 21.061 60. 889 1. 00 55. 85 ATOM 92 N **GLN 26** 43. 519 21. 563 60.399 1. 00 58. 22 ATOM 93 CA **GLN 26** 43. 527 22. 807 61. 153 1. 00 58. 31 15 ATOM 94 CB **GLN 26** 44. 980 23. 280 61.361 1. 00 63. 03 ATOM 95 CG **GLN 26** 45. 118 24. 480 62. 313 1. 00 69. 87 ATOM 96 CD **GLN 26** 46. 490 25. 161 62. 245 1. 00 73. 70 ATOM 97 OE1 GLN 26 47.009 25. 446 61. 158 1.00 74.68 ATOM NE2 GLN 26 98 47.067 25. 446 63. 411 1.00 74.99 20 ATOM 99 C **GLN 26** 42. 702 23.903 60. 485 1. 00 55. 29 ATOM 100 **GLN 26** 0 42. 358 23.811 59. 308 1. 00 51. 30 ATOM **GLU 27** 101 N 42. 389 24. 931 61. 267 1. 00 55. 08 ATOM 102 GLU 27 CA 41.617 26.083 60.824 1.00 55.66 ATOM 103 **GLU 27** CB41.940 27. 280 61. 709 1. 00 57. 13 25 ATOM 104 CG GLU 27 41.029 28. 469 61. 523 1.00 59.64 ATOM 105 CD GLU 27 39.694 28. 272 62. 208 1. 00 62. 00 ATOM 106 0E1 GLU 27 39. 685 27.840 63. 382 1. 00 62. 44 ATOM 107 0E2 GLU 27 38. 653 28. 559 61.581 1. 00 64. 27

ATOM

C

GLU 27

41. 905

26. 454

59. 380

1. 00 55. 70

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	ATOM	109	0	GLU	27	41.025	26. 416	58. 531	1. 00	56. 30
	ATOM	110	N	GLU	28	43. 147	26. 828	59. 113	1. 00	56. 74
	ATOM	111	CA	GLU	28	43. 571	27. 208	57. 770	1. 00	58. 34
	ATOM	112	CB	GLU	28	45. 102	27. 226	57. 714	1. 00	63. 94
5	ATOM	113	CG	GLU	28	45. 704	28. 026	56. 573	1. 00	70. 36
	ATOM	114	CD	GLU	28	45. 615	29. 524	56. 806	1. 00	74. 74
	ATOM	115	0E1	GLIJ	28	46. 245	30. 289	56. 040	1. 00	77. 18
	ATOM	116	0E2	GLU	28	44. 912	29. 938	57. 755	1. 00	77. 44
	ATOM	117	C	GLU	28	43. 032	26. 231	56. 721	1. 00	56. 56
10	ATOM	118	0 ·	GLU	28	42. 375	26. 641	55. 764	1. 00	54. 38
	ATOM	119	N	ASP	29	43. 316	24. 942	56. 921	1. 00	55. 20
	ATOM	120	CA	ASP	29	42. 893	23. 869	56. 015	1. 00	53. 13
	ATOM	121	CB	ASP	29	43. 106	22. 499	56. 667	1. 00	56. 36
	ATOM	122	CG	ASP	29	44. 570	22. 116	56. 758	1. 00	59. 69
15	ATOM	123	OD 1	ASP	29	45. 263	22. 198	55. 717	1. 00	61. 07
	ATOM	124	OD2	ASP	29	45. 021	21. 727	57. 863	1. 00	60. 92
	ATOM	125	C	ASP	29	41. 439	23. 995	55. 607	1. 00	49. 74
	ATOM	126	0	ASP	29	41. 100	23. 924	54. 424	1. 00	47. 81
	ATOM	127	N	LEU	30	40. 579	24. 156	56. 603	1. 00	46. 04
20	ATOM	128	CA	LEU	30	39. 167	24. 309	56. 344	1. 00	43. 06
	ATOM	129	CB	LEU	30	38. 393	24. 491	57. 649	1. 00	39. 08
	ATOM	130	CG	LEU	30	38. 026	23. 218	58. 404	1. 00	36. 61
	ATOM	131	CD1	LEU	30	39. 280	22. 441	58. 756	1. 00	37. 28
	ATOM	132	CD2	LEU	30	37. 233	23. 576	59. 642	1. 00	35. 29
25	ATOM	133	C	LEU	30	38. 948	25. 516	55. 452	1. 00	44. 18
	ATOM	134	0	LEU	30	38. 410	25. 388	54. 354	1. 00	45. 60
	ATOM	135	N	LYS	31	39. 381	26. 685	55. 920	1. 00	44. 63
	ATOM	136	CA	LYS	31	39. 206	27. 927	55. 170	1. 00	43. 67
	ATOM	137	CB	LYS	31	40. 136	29. 020	55. 695	1. 00	45. 23

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	ATOM	138	CG	LYS	31	39. 968	29. 361	57. 165	1. 00 46. 98
	ATOM	139	CD	LYS	31	38. 743	30. 221	57. 440	1. 00 45. 54
	ATOM	140	CE	LYS	31	38. 695	30. 675	58. 915	1. 00 45. 82
	ATOM	141	NZ	LYS	31	39. 836	31. 545	59. 387	1. 00 42. 73
5	ATOM	142	C	LYS	31	39. 483	27. 725	53. 697	1. 00 42. 23
	ATOM	143	0	LYS	31	38. 759	28. 241	52. 855	1. 00 41. 29
	ATOM	144	N	LYS	32	40. 535	26. 976	53. 385	1. 00 41. 79
	ATOM	145	CA	LYS	32	40. 877	26. 737	51. 994	1. 00 43. 47
	ATOM	146	CB	LYS	32	42. 171	25. 928	51. 888	1. 00 45. 16
10	ATOM	147	CG	LYS	32	42. 811	25. 974	50. 499	1. 00 50. 49
	ATOM	148	CD	LYS	32	44. 302	25. 565	50. 510	1. 00 54. 48
	ATOM	149	CE	LYS	32	44. 505	24. 086	50. 900	1. 00 57. 45
	ATOM	150	NZ	LYS	32	45. 934	23. 610	51. 002	1. 00 56. 65
	ATOM	151	C	LYS	32	39. 740	25. 995	51. 308	1. 00 43. 99
15	ATOM	152	0	LYS	32	39. 260	26. 407	50. 246	1. 00 43. 34
	ATOM	153	N	VAL	33	39. 306	24. 901	51. 925	1. 00 43. 47
	ATOM	154	CA	VAL	33	38. 218	24. 100	51. 382	1. 00 40. 87
	ATOM	155	CB	VAL	33	37. 895	22. 927	52. 310	1. 00 40. 53
	ATOM	156	CG1	VAL	33	36. 977	21. 939	51. 604	1. 00 40. 20
20	ATOM	157	CG2	VAL	33	39. 183	22. 248	52. 729	1. 00 40. 29
	ATOM	158	C	VAL	33	36. 994	24. 981	51. 226	1. 00 39. 39
	ATOM	159	0	VAL	33	36. 370	25. 011	50. 165	1. 00 37. 22
	ATOM	160	N	MET	34	36. 675	25. 707	52. 290	1. 00 39. 46
	ATOM	161	CA	MET	34	35. 539	26. 609	52. 288	1. 00 42. 17
25	ATOM	162	CB	MET	34	35. 515	27. 460	53. 555	1. 00 43. 81
	ATOM	163	CG	MET	34	34. 259	28. 305	53. 656	1. 00 48. 81
	ATOM	164	SD	MET	34	34. 302	29. 606	54. 908	1. 00 56. 60
	ATOM	165	CE	MET	34	34. 576	31. 074	53. 859	1. 00 55. 54
	ATOM	166	C	MET	34	35. 612	27. 535	51. 086	1. 00 43. 35

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	ATOM	167	0	MET	34	34. 626	27. 735	50. 383	1. 00 43. 86
	ATOM	168	N	ARG	35	36. 785	28. 104	50. 847	1. 00 44. 90
	ATOM	169	CA	ARG	35	36. 938	29. 015	49. 729	1. 00 45. 60
	ATOM	170	CB	ARG	35	38. 286	29. 727	49. 815	1. 00 49. 40
5	ATOM	171	CG	ARG	35	38. 459	30. 563	51. 075	1. 00 53. 81
	ATOM	172	CD	ARG	35	38. 231	32. 052	50. 851	1. 00 57. 78
	ATOM	173	NE	ARG	35	38. 483	32. 807	52. 077	1. 00 63. 20
	ATOM	174	CZ	ARG	35	39. 587	32. 696	52. 820	1. 00 65. 30
	ATOM	175	NH 1	ARG	35	40. 557	31. 854	52. 466	1. 00 64. 80
10	ATOM	176	NH2	ARG	35	39. 720	33. 425	53. 925	1. 00 66. 89
	ATOM	177	C	ARG	35	36. 814	28. 262	48. 418	1. 00 44. 08
	ATOM	178	0	ARG	35	35. 977	28. 605	47. 586	1. 00 43. 75
	ATOM	179	N	ARG	36	37. 633	27. 227	48. 245	1. 00 43. 43
	ATOM	180	CA	ARG	36	37. 612	26. 418	47. 026	1. 00 43. 94
15	ATOM	181	CB	ARG	36	38. 547	25. 212	47. 174	1. 00 44. 76
	ATOM	182	CG	ARG	36	40. 020	25. 580	47. 244	1. 00 44. 66
	ATOM	183	CD	ARG	36	40. 898	24. 392	47. 617	1. 00 44. 20
	ATOM	184	NE	ARG	36	41. 728	23. 919	46. 512	1. 00 44. 66
	ATOM	185	CZ	ARG	36	42. 890	23. 292	46. 678	1. 00 45. 10
20	ATOM	186	NH1	ARG	36	43. 350	23. 075	47. 900	1. 00 44. 34
	ATOM	187	NH2	ARG	36	43. 590	22. 870	45. 631	1. 00 45. 47
	ATOM	188	C	ARG	36	36. 202	25. 941	46. 660	1. 00 43. 73
	ATOM	189	0	ARG	36	35. 921	25. 645	45. 497	1. 00 43. 31
	ATOM	190	N	MET	37	35. 324	25. 851	47. 656	1. 00 42. 87
25	ATOM	191	CA	MET	37	33. 946	25. 440	47. 413	1. 00 41. 30
	ATOM	192	CB	MET	37	33. 222	25. 136	48. 726	1. 00 43. 30
	ATOM	193	CG	MET	37	31. 782	24. 636	48. 556	1. 00 45. 16
	ATOM	194	SD	MET	37	31. 646	22. 826	48. 280	1. 00 52. 61
	ATOM	195	CE	MET	37	31. 892	22. 708	46. 492	1. 00 46. 47

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	ATOM	196	С	MEI	37	33. 249	26. 603	46. 723	1. 00 39. 52
	ATOM	197	0	MET	37	32. 702	26. 458	45. 635	1. 00 39. 06
	ATOM	198	N	GLN	38	33. 275	27. 767	47. 359	1. 00 37. 22
	ATOM	199	CA	GLN	38	32. 637	28. 927	46. 776	1. 00 35. 67
5	ATOM	200	CB	GLN	38	32. 874	30. 155	47. 643	1. 00 36. 29
	ATOM	201	CG	GLN	38	32. 128	30. 122	48. 950	1. 00 37. 44
	ATOM	202	CD	GLN	38	32. 689	31. 108	49. 950	1. 00 41. 99
	ATOM	203	0E	1 GLN	38	33. 841	30. 992	50. 376	1. 00 44. 33
	ATOM	204	NE2	2 GLN	38	31. 880	32. 091	50. 331	1. 00 44. 58
10	ATOM	205	C	GLN	38	33. 184	29. 155	45. 382	1. 00 35. 21
	ATOM	206	0	GLN	38	32. 454	29. 557	44. 486	1. 00 34. 82
	ATOM	207	N	LYS	39	34. 467	28. 884	45. 188	1. 00 36. 41
	ATOM	208	CA	LYS	39	35. 069	29. 081	43. 875	1. 00 38. 60
	ATOM	209	CB	LYS	39	36. 560	28. 708	43. 888	1. 00 42. 47
15	ATOM	210	CG	LYS	39	37. 395	29. 263	42. 714	1. 00 45. 02
	ATOM	211	CD	LYS	39	37. 638	30. 775	42. 861	1. 00 49. 54
	ATOM	212	CE	LYS	39	38. 523	31. 365	41. 752	1. 00 51. 65
	ATOM	213	NZ	LYS	39	38. 621	32. 865	41. 821	1. 00 53. 58
	ATOM	214	C	LYS	39	34. 339	28. 196	42. 884	1. 00 38. 31
20	ATOM	215	0	LYS	39	34. 229	28. 534	41.710	1. 00 40. 28
	ATOM		N	GLU		33. 827	27. 066	43. 369	1. 00 37. 21
	ATOM	217	CA	GLU	40	33. 117	26. 107	42. 525	1. 00 34. 69
	ATOM	218	CB	GLU	40	33. 329	24. 705	43. 072	1. 00 32. 80
	ATOM	219	CG	GLU	40	34. 742	24. 245	42. 900	1. 00 33. 53
25	ATOM	220	CD	GLU	40	35. 164	24. 348	41. 459	1. 00 36. 48
	ATOM	221	0E1	GLU	40	34. 318	24. 044	40. 589	1. 00 39. 36
	ATOM	222	0E2	GLU	40	36. 326	24. 720	41. 187	1. 00 37. 18
	ATOM	223	C	GLU	40	31. 632	26. 387	42. 375	1. 00 34. 48
	ATOM	224	0	GLU	40	31. 040	26. 110	41. 332	1. 00 32. 30

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	ATOM	225	N	MET	41	31. 03	0 26. 928	43. 425	1. 00 35. 61
	ATOM	226	CA	MET	41	29. 62	27. 256	43. 373	1. 00 39. 30
	ATOM	227	CB	MET	41	29. 15	5 27. 852	44. 692	1. 00 39. 16
	ATOM	228	CG	MET	41	29. 14	6 26. 910	45. 867	1. 00 40. 71
5	ATOM	229	SD	MET	41	27. 93	0 27. 569	47. 040	1. 00 46. 34
	ATOM	230	CE	MET	41	28. 97	8 28. 338	48. 243	1. 00 46. 54
	ATOM	231	C	MET	41	29. 33	6 28. 258	42. 251	1. 00 42. 24
	ATOM	232	0	MET	41	28. 35	8 28. 113	41. 517	1. 00 44. 97
	ATOM	233	N	ASP	42	30. 17	3 29. 284	42. 118	1. 00 43. 47
10	ATOM	234	CA	ASP	42	29. 95	2 30. 274	41. 069	1. 00 42. 69
	ATOM	235	CB	ASP	42	30. 84	8 31. 497	41. 249	1. 00 44. 70
	ATOM	236	CG	ASP	42	30. 54	8 32. 254	42. 523	1. 00 49. 63
	ATOM	237	0D1	ASP	42	31. 35	2 32. 128	43. 477	1. 00 52. 14
	ATOM	238	0D2	ASP	42	29. 51	0 32. 968	42. 572	1. 00 49. 66
15	ATOM	239	C	ASP	42	30. 24	8 29.641	39. 739	1. 00 41. 40
	ATOM	240	0	ASP	42	29. 55	0 29. 880	38. 759	1. 00 41. 06
	ATOM	241	N	ARG	43	31. 28	9 28. 826	39. 707	1. 00 39. 70
	ATOM	242	CA	ARG	43	31. 66	8 28. 171	38. 477	1. 00 39. 99
	ATOM	243	CB	ARG	43	32. 83	5 27. 227	38. 739	1. 00 43. 98
20	ATOM	244	CG	ARG	43	33. 32	9 26. 482	37. 516	1. 00 49. 72
	ATOM	245	CD	ARG	43	34. 63	6 25. 777	37. 831	1. 00 55. 67
	ATOM	246	NE	ARG	43	34. 96	2 24. 746	36. 854	1. 00 62. 98
	ATOM	247	CZ	ARG	43	36. 06	2 24. 002	36. 899	1. 00 67. 95
	ATOM	248	NH1	ARG	43	36. 95	0 24. 178	37. 877	1. 00 69. 41
25	ATOM	249	NH2	ARG	43	36. 26	9 23. 075	35. 969	1. 00 70. 32
	ATOM	250	C	ARG	43	30. 488	3 27. 417	37. 881	1. 00 38. 35
	ATOM	251	0	ARG	43	30. 253	3 27. 493	36. 677	1. 00 38. 07
	ATOM	252	N	GLY	44	29. 739	26. 709	38. 728	1. 00 36. 44
	ATOM	253	CA	GLY	44	28. 592	2 25. 938	38. 262	1. 00 32. 80

- 153 -ATOM 254 C GLY 44 27. 344 26. 772 38. 062 1. 00 31. 71 ATOM 255 0 GLY 44 26. 483 26. 448 37. 251 1. 00 30. 43 ATOM 256 N LEU 45 27. 258 38. 820 27. 854 1.00 31.23 **ATOM** 257 CA LEU 45 26. 144 28. 774 38. 761 1. 00 31. 72 ATOM 258 CB LEU 45 5 26. 168 29.638 40.010 1. 00 30. 96 ATOM 259 CG LEU 45 25. 063 29.363 41. 013 1. 00 34. 38 ATOM 260 CD1 LEU 45 25. 346 30.066 42. 334 1. 00 34. 74 **ATOM** 261 CD2 LEU 45 23. 750 29. 849 40. 413 1. 00 37. 12 ATOM 262 C LEU 45 26. 204 29.666 37. 517 1. 00 33. 39 10 ATOM 263 0 LEU 45 25. 184 30. 211 37. 086 1. 00 34. 01 ATOM 264 N ARG 46 27. 402 29. 813 36. 955 1. 00 34. 39 ATOM 265 CA ARG 46 27.628 30. 651 35. 774 1. 00 37. 39 ATOM 266 CBARG 46 29. 092 31. 140 35. 744 1. 00 42. 80 **ATOM** 267 CG ARG 46 29.463 32. 067 34. 562 1. 00 48. 17 15 ATOM 268 CDARG 46 30. 951 32. 487 34. 546 1. 00 49. 35 **ATOM** 269 NE ARG 46 31. 250 33. 400 33. 441 1. 00 54. 04 CZATOM 270 ARG 46 30. 599 34. 542 33. 216 1. 00 57. 98 ATOM 271 NH1 ARG 46 29.608 34. 915 34.019 1. 00 56. 34 ATOM 272 NH2 ARG 46 30. 936 35. 316 32. 187 1. 00 59. 91 20 ATOM 273 C ARG 46 27. 301 29. 920 34. 477 1. 00 37. 53 ATOM 274 0 ARG 46 27. 773 28. 804 34. 243 1. 00 38. 11 ATOM 275 N LEU 47 26. 515 30. 573 33.623 1.00 36.42 ATOM 276 CA LEU 47 26. 089 29. 993 32. 350 1.00 35.82 ATOM 277 CB LEU 47 25. 151 30. 957 31. 617 1. 00 31. 45 **ATOM** 25 278 CG LEU 47 24. 771 30. 548 30. 196 1. 00 29. 68 ATOM 279 CD1 LEU 47 24. 031 29. 240 30. 230 1. 00 28. 93 ATOM 280 CD2 LEU 47 23. 929 31. 622 29. 559 1. 00 28. 83 ATOM 281 C LEU 47 27. 223 29. 578 31. 418 1. 00 37. 14

ATOM

282

0

LEU 47

27. 152

28. 534

30. 764 1. 00 36. 41

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	ATOM	283	N	GLU	48	28. 272	30. 383	31. 347	1. 00 39. 28
	ATOM	284	CA	GLU	48	29. 371	30. 034	30. 462	1. 00 42. 38
	ATOM	285	CB	GLU	48	30. 448	31. 126	30. 473	1. 00 43. 91
	ATOM	286	CG	GLU	48	30. 126	32. 354	29. 631	1. 00 46. 02
5	ATOM	287	CD	GLU	48	29. 022	33. 215	30. 221	1. 00 48. 71
	ATOM	288	0E1	GLU	48	28. 581	34. 157	29. 524	1. 00 48. 10
	ATOM	289	0E2	GLU	48	28. 600	32. 959	31. 375	1. 00 49. 31
	ATOM	290	C	GLU	48	30. 005	28. 691	30. 809	1. 00 43. 42
	ATOM	291	0	GLU	48	30. 593	28. 045	29. 939	1. 00 43. 61
10	ATOM	292	N	THR	49	29. 873	28. 262	32. 066	1. 00 44. 28
	ATOM	293	CA	THR	49	30. 484	26. 999	32. 508	1. 00 46. 81
	ATOM	294	CB	THR	49	31. 761	27. 267	33. 366	1. 00 47. 70
	ATOM	295	0G1	THR	49	31. 477	28. 265	34. 356	1. 00 45. 18
	ATOM	296	CG2	THR	49	32. 921	27. 739	32. 486	1. 00 48. 17
15	ATOM	297	C	THR	49	29. 595	26. 024	33. 293	1. 00 46. 50
	ATOM	298	0	THR	49	30. 043	24. 932	33. 683	1. 00 45. 72
	ATOM	299	N	HIS	50	28. 340	26. 405	33. 508	1. 00 44. 18
	ATOM	300	CA	HIS	50	27. 416	25. 565	34. 262	1. 00 41. 93
	ATOM	301	CB	HIS	50	25. 980	26. 129	34. 190	1. 00 38. 83
20	ATOM	302	CG	HIS	50	25. 217	25. 754	32. 953	1. 00 35. 50
	ATOM	303	CD2	HIS	50	23. 950	25. 304	32. 795	1. 00 33. 70
	ATOM	304	ND1	HIS	50	25. 730	25. 894	31. 682	1. 00 36. 24
	ATOM	305	CE1	HIS	50	24. 812	25. 550	30. 796	1. 00 33. 56
	ATOM	306	NE2	HIS	50	23. 722	25. 189	31. 446	1. 00 32. 06
25	ATOM	307	C	HIS	50	27. 447	24. 117	33. 804	1. 00 41. 73
	ATOM	308	0	HIS	50	27. 144	23. 212	34. 572	1. 00 41. 14
	ATOM	309	N	GLU	51	27. 848	23. 883	32. 566	1. 00 42. 00
	ATOM	310	CA	GLU	51	27. 863	22. 519	32. 103	1. 00 45. 79
	ATOM	311	CB	GLU	51	27. 573	22. 463	30. 617	1. 00 46. 76

- 155 -ATOM 312 CG **GLU 51** 27. 523 21. 048 30. 100 1. 00 50. 98 ATOM 313 CD GLU 51 26. 521 20. 885 28. 989 1. 00 53. 94 ATOM 314 0E1 GLU 51 25. 313 21.082 29. 253 1. 00 55. 61 ATOM 315 0E2 GLU 51 26. 940 20.560 27. 857 1. 00 55. 48 ATOM 5 316 C GLU 51 29. 139 21. 757 32. 402 1. 00 48. 17 ATOM 317 0 **GLU 51** 29. 094 20. 657 32. 953 1. 00 49. 35 ATOM 318 N GLU 52 30. 276 22. 331 32. 034 1. 00 50. 75 **ATOM** 319 CA GLU 52 31. 565 21. 681 32. 264 1. 00 52. 07 ATOM 320 CBGLU 52 32. 633 22. 321 31. 352 1. 00 56. 66 10 ATOM 321 CG GLU 52 32. 768 23. 854 31.476 1. 00 63. 81 ATOM 322 CD GLU 52 33. 420 24. 528 30. 253 1. 00 67. 84 ATOM 323 OE1 GLU 52 33. 601 25. 770 30. 278 1. 00 68. 83 ATOM 324 0E2 GLU 52 33. 742 23.826 29. 266 1. 00 70.00 ATOM 325 C GLU 52 31. 982 21.760 33. 738 1. 00 49. 95 ATOM 15 326 0 GLU 52 33. 013 21. 215 34. 132 1. 00 47. 47 ATOM ALA 53 327N 31. 162 22. 429 34. 548 1. 00 48. 46 ATOM 328 CA ALA 53 31. 449 22. 594 35. 972 1. 00 47. 88 ATOM 329 CB ALA 53 30. 418 23. 510 36. 615 1. 00 47. 30 ATOM 330 C ALA 53 31. 510 21. 278 36. 731 1. 00 46. 84 20 ATOM 331 0 ALA 53 31. 287 20. 206 36. 172 1. 00 48. 51 ATOM 332N SER 54 31. 816 21. 353 38.016 1. 00 44. 67 ATOM 333 CA SER 54 31. 895 20. 133 38. 792 1. 00 42. 38 ATOM 334 CB SER 54 33. 201 20.090 39. 581 1. 00 44. 26 ATOM 335 0G SER 54 33. 290 18. 883 40. 316 1. 00 45. 49 25 ATOM 336 С SER 54 30. 712 20.059 39. 734 1. 00 39. 72 **ATOM** 337 0 SER 54 30.058 19.028 39. 841 1.00 41.09 **ATOM** 338 N VAL 55 30. 440 21. 165 40. 411 1. 00 34. 77

ATOM

ATOM

339

340

CA

CB

VAL 55

VAL 55

29. 326

29. 682

21. 239

22. 186

41. 343

42. 498

1. 00 30. 58

1. 00 28. 73

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	ATOM	341	CG1	VAL	55	28. 480	22. 433	43. 383	1. 00	30. 75
	ATOM	342	CG2	VAL	55	30. 814	21. 596	43. 297	1. 00	25. 80
	ATOM	343	C	VAL	55	28. 094	21. 760	40. 597	1. 00	30. 28
	ATOM	344	0	VAL	55	27. 704	22. 920	40. 745	1. 00	32. 16
5	ATOM	345	N	LYS	56	27. 482	20. 887	39. 803	1. 00	26. 82
	ATOM	346	CA	LYS	56	26. 323	21. 235	38. 986	1. 00	21. 66
	ATOM	347	CB	LYS	56	25. 362	20. 046	38. 891	1. 00	26. 53
	ATOM	348	CG	LYS	56	25. 936	18. 737	38. 337	1. 00	29. 32
	ATOM	349	CD	LYS	56	26. 311	18. 836	36. 875	1. 00	29. 86
10	ATOM	350	CE	LYS	56	27. 609	19. 592	36. 698	1. 00	29. 73
	ATOM	351	NZ	LYS	56	27. 932	19. 759	35. 259	1. 00	32. 80
	ATOM	352	C	LYS	56	25. 520	22. 470	39. 374	1. 00	17. 56
	ATOM	353	0	LYS	56	25. 133	23. 236	38. 498	1. 00	15. 95
	ATOM	354	N	MET	57	25. 257	22. 660	40. 665	1. 00	14. 30
15	ATOM	355	CA	MET	57	24. 462	23. 803	41. 128	1. 00	12. 73
	ATOM	356	CB	MET	57	25. 277	25. 089	41. 059	1. 00	9. 92
	ATOM	357	CG	MET	57	26. 515	25. 090	41. 930	1. 00	6. 47
	ATOM	358	SD	MET	57	26. 219	25. 164	43. 694	1. 00	8. 00
	ATOM	359	CE	MET	57	25. 523	26. 842	43. 905	1. 00	1. 00
20	ATOM	360	C	MET	57	23. 207	23. 953	40. 270	1. 00	14. 05
	ATOM	361	0	MET	57	23. 000	24. 972	39. 610	1. 00	12. 36
	ATOM	362	N	LEU	58	22. 371	22. 923	40. 290	1. 00	17. 80
	ATOM	363	CA	LEU	58	21. 154	22. 914	39. 498	1. 00	19. 02
	ATOM	364	CB	LEU	58	20. 710	21. 466	39. 245	1. 00	18. 03
25	ATOM	365	CG	LEU	58	21. 726	20. 444	38. 720	1. 00	16. 28
	ATOM	366	CD1	LEU	58	21. 193	19. 068	39. 021	1. 00	20. 44
	ATOM	367	CD2	LEU	58	21. 999	20. 608	37. 233	1. 00	15. 03
	ATOM	368	C	LEU	58	20. 005	23. 696	40. 134	1. 00	20. 20
	ATOM	369	0	LEU	58	19. 752	23. 602	41. 340	1. 00	19. 91

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ATOM 370 N PRO 59 19. 316 24. 507 39. 320 1. 00 20. 57 ATOM 371 CD PRO 59 19.856 24. 939 38. 022 1. 00 20. 39 ATOM 372 CA PRO 59 18. 171 25. 342 39. 694 1. 00 22. 50 ATOM 373 CBPRO 59 17.939 26. 168 38. 437 1. 00 22. 07 5 ATOM 374 CG PRO 59 19. 306 26. 329 37. 906 1. 00 21. 92 ATOM 375 C PRO 59 16. 975 24. 437 40.010 1.00 23.49 ATOM 376 0 PRO 59 16.698 23. 504 39. 264 1. 00 25. 36 ATOM 377 N **THR 60** 16. 258 24. 714 41.092 1. 00 22. 35 ATOM 378 CA THR 60 15. 133 23.871 41.469 1. 00 20. 99 10 ATOM 379 CB THR 60 15. 097 23.607 42.964 1. 00 22. 35 ATOM 380 OG1 THR 60 14. 823 24. 837 43. 647 1. 00 24. 53 ATOM 381 CG2 THR 60 23. 049 16. 408 43. 441 1. 00 24. 88 ATOM 382 C THR 60 13. 815 24. 516 41. 160 1. 00 20. 21 ATOM 383 0 THR 60 12. 793 23.848 41. 119 1. 00 24. 18 15 ATOM 384 N TYR 61 13. 839 25. 822 40. 973 1.00 19.09 ATOM 385 CA TYR 61 12. 628 26. 595 40. 715 1. 00 20. 03 **ATOM** 386 CBTYR 61 11.955 26. 172 39. 427 1. 00 13. 50 **ATOM** 387 CG TYR 61 12. 581 26. 830 38. 234 1. 00 13. 18 ATOM 388 CD1 TYR 61 12.028 27. 983 37. 666 1. 00 8. 00 ATOM 20 389 CE1 TYR 61 12. 596 28. 551 36. 536 1. 00 4. 24 ATOM 390 CD2 TYR 61 13. 725 26. 281 37. 647 1.00 14.04 ATOM 391 CE2 TYR 61 14. 296 26. 843 36. 529 1.00 10.05 ATOM 392 CZTYR 61 13. 730 27.963 35. 976 1.00 5.80 ATOM 393 OH TYR 61 14. 307 28. 423 34. 828 1.00 4.54 ATOM 25 394 C TYR 61 11.620 26.572 41. 833 1. 00 21. 95 ATOM 395 0 TYR 61 10. 437 26. 816 41.609 1. 00 22. 47 ATOM 396 N VAL 62 12. 102 26. 293 43. 037 1. 00 24. 47 ATOM 397 CA VAL 62 11. 265 26. 288 44. 218 1. 00 29. 86 ATOM 398 CB VAL 62 11.750 25. 231 45. 207 1. 00 28. 92

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	ATOM	399	CG	l VAI	62	10. 780	25. 091	46. 370	1. 00 28. 30
	ATOM	400	CG	VAI	62	11. 909	23. 926	44. 480	1. 00 28. 58
	ATOM	401	C	VAI	62	11. 494	27. 680	44. 786	1. 00 34. 67
	ATOM	402	0	VAL	62	11. 584	27. 879	45. 993	1. 00 39. 01
5	ATOM	403	N	ARG	63	11. 589	28. 638	43. 874	1. 00 38. 40
	ATOM	404	CA	ARG	63	11. 847	30. 038	44. 182	1. 00 41. 10
	ATOM	405	CB	ARG	63	12. 041	30. 804	42. 874	1. 00 42. 02
	ATOM	406	CG	ARG	63	10. 794	30. 798	41. 996	1. 00 44. 76
	ATOM	407	CD	ARG	63	11. 072	31. 197	40. 550	1. 00 46. 61
10	ATOM	408	NE	ARG	63	9. 827	31. 366	39. 804	1. 00 48. 56
	ATOM	409	CZ	ARG	63	8. 972	30. 381	39. 541	1. 00 50. 39
	ATOM	410	NH 1	ARG	63	9. 225	29. 145	39. 955	1. 00 50. 83
	ATOM	411	NH2	ARG	63	7. 854	30. 635	38. 875	1. 00 51. 11
	ATOM	412	C	ARG	63	10. 788	30. 751	45. 004	1. 00 42. 71
15	ATOM	413	0	ARG	63	9. 790	30. 167	45. 424	1. 00 41. 58
	ATOM	414	N	SER	64	11. 047	32. 036	45. 224	1. 00 46. 12
	ATOM	415	CA	SER	64	10. 155	32. 922	45. 954	1. 00 49. 96
	ATOM	416	CB	SER	64	10. 400	32. 826	47. 454	1. 00 50. 57
	ATOM	417	0G	SER	64	9. 374	33. 507	48. 157	1. 00 53. 70
20	ATOM	418	C	SER	64	10. 435	34. 340	45. 458	1. 00 51. 04
	ATOM	419	0	SER	64	11. 300	35. 047	45. 985	1. 00 50. 38
	ATOM	420	N	THR	65	9. 690	34. 728	44. 425	1. 00 53. 23
	ATOM	421	CA	THR	65	9. 827	36. 031	43. 791	1. 00 54. 89
	ATOM	422	CB	THR	65	10. 151	35. 871	42. 281	1. 00 56. 21
25	ATOM	423	0G1	THR	65	9. 094	35. 158	41. 622	1. 00 55. 23
	ATOM	424	CG2	THR		11. 461	35. 112	42. 103	1. 00 56. 71
	ATOM	425	C	THR		8. 582	36. 911	43. 939	1. 00 56. 01
	ATOM	426	0	THR		7. 503	36. 430	44. 291	1. 00 56. 26
	ATOM	427	N	PRO	66	8. 728	38. 222	43. 676	1. 00 56. 49

- 159 -ATOM 428 CD PRO 66 10. 019 38.866 43. 377 1.00 56.96 ATOM 429 CA PRO 66 7. 666 39. 228 43. 758 1. 00 56. 28 ATOM 430 CB PRO 66 8.369 40.502 43. 313 1.00 57.08 ATOM 431 CG PRO 66 9. 759 40. 287 43. 786 1. 00 58. 08 ATOM 432 C PRO 66 5 6. 487 38.901 42.864 1. 00 56. 75 ATOM 433 0 PRO 66 5. 477 39.604 42.874 1. 00 57. 23 ATOM 434 N GLU 67 6. 631 37.849 42.072 1.00 56.42 ATOM 435 CA GLU 67 5. 540 41. 193 37. 445 1. 00 56. 82 ATOM 436 CB GLU 67 6. 048 36. 487 40. 115 1. 00 61. 19 ATOM 437 CG **GLU 67** 10 6. 421 35. 108 40. 637 1.00 66.99 ATOM 438 CD GLU 67 7. 123 34. 261 39. 594 1. 00 69. 61 ATOM 439 0E1 GLU 67 8. 253 39. 201 34. 618 1. 00 70. 19 0E2 GLU 67 ATOM 440 6. 541 33. 241 39. 168 1.00 70.18 ATOM 441 C **GLU 67** 4. 406 36.803 41. 984 1.00 54.30 ATOM 442 15 0 GLU 67 3. 241 36.940 41. 633 1. 00 54. 25 ATOM 443 N GLY 68 4. 753 36. 116 43. 076 1. 00 50. 50 ATOM 444 CA GLY 68 3. 741 35. 478 43. 901 1. 00 45. 77 ATOM 445 C **GLY 68** 4. 166 44. 316 34.087 1. 00 43. 04 ATOM 446 0 **GLY 68** 3. 626 33. 503 45. 259 1. 00 40. 69 20 ATOM 447 N **SER 69** 5. 154 33. 564 43. 599 1. 00 42. 30 ATOM 448 CA **SER 69** 5. 690 43. 845 32. 230 1. 00 41. 02 **ATOM** 449 CB**SER 69** 6.769 31. 902 42. 804 1. 00 41. 03 **ATOM** 450 0G **SER 69** 6. 438 41.517 32. 404 1. 00 42. 34 ATOM 451 C **SER 69** 6. 301 32. 126 45. 240 1. 00 39. 68 25 ATOM 452 0 **SER 69** 7. 163 32. 920 45. 607 1. 00 38. 89 ATOM 453 N **GLU 70** 5. 857 46.014 31. 143 1. 00 39. 96 **ATOM** 454 CA **GLU 70** 6.388 30. 942 47. 355 1. 00 40. 53 ATOM 455 CB**GLU 70** 5. 265 31.074 48. 391 1. 00 44. 80

ATOM

456

CG

GLU 70

4.675

32. 483

48. 492

1. 00 52. 74

- 160 -ATOM 457 CD **GLU 70** 5. 705 33. 554 48. 900 1. 00 58. 55 0E1 GLU 70 ATOM 458 5. 362 34. 763 48. 866 1. 00 59. 55 ATOM 459 0E2 GLU 70 6. 852 33. 192 49. 258 1. 00 60. 30 **GLU** 70 ATOM 460 C 7.075 29. 583 47. 483 1. 00 38. 65 ATOM **GLU 70** 5 461 0 6.807 28.660 46. 704 1.00 37.89 **ATOM** 462 N VAL 71 7. 962 29. 459 48. 466 1.00 35.96 **ATOM** 463 CA VAL 71 8. 670 28. 207 48. 653 1. 00 34. 46 ATOM 464 CB VAL 71 28. 319 9. 723 49.755 1.00 33.00 ATOM 465 CG1 VAL 71 10. 236 26. 949 50. 120 1. 00 33. 91 10 ATOM CG2 VAL 71 466 10. 885 29. 152 49. 249 1. 00 32. 56 ATOM 467 C VAL 71 7. 730 27. 042 48. 931 1.00 34.75 ATOM 468 0 VAL 71 7. 851 25. 985 48. 310 1. 00 37. 23 ATOM 469 N **GLY** 72 6. 783 27. 219 49. 841 1. 00 33. 37 ATOM 470 CA GLY 72 5. 842 26. 139 50. 105 1.00 32.39 ATOM 15 471 **GLY** 72 C 5.066 25. 644 48. 879 1.00 31.10 ATOM 472 0 **GLY 72** 4. 631 24. 493 48. 859 1. 00 28. 98 ATOM 473 N ASP 73 4. 878 26. 503 47.870 1.00 31.05 **ATOM** 474 CA ASP 73 4. 156 26. 129 46.650 1. 00 31. 14 **ATOM** 475 CB ASP 73 4. 389 27. 147 45. 532 1.00 34.00 20 ATOM 476 ASP 73 CG 3. 759 28. 491 45.817 1. 00 38. 43 **ATOM** 477 OD1 ASP 73 29.355 3. 758 44. 907 1.00 41.88 **ATOM** 478 OD2 ASP 73 3. 262 28. 690 46. 945 1.00 41.23 ATOM 479 C ASP 73 4.675 24. 785 46. 189 1. 00 30. 89 **ATOM** 480 0 ASP 73 5. 875 24. 544 46. 256 1.00 32.81 25 ATOM 481 N PHE 74 3. 796 23.921 45. 694 1. 00 28. 84 ATOM 482 CA PHE 74 4. 233 22. 595 45. 271 1. 00 27. 21 ATOM 483 CBPHE 74 4. 728 21. 834 46. 502 1. 00 26. 13 **ATOM** 484 CG PHE 74 5. 407 20. 551 46. 185 1. 00 25. 61 ATOM 485 CD1 PHE 74 6. 641 20. 546 45. 547 1. 00 29. 29

- 161 -ATOM 486 CD2 PHE 74 4. 805 19. 344 46. 496 1. 00 24. 94 ATOM CE1 PHE 74 487 7. 259 19. 354 45. 213 1.00 31.36 ATOM CE2 PHE 74 488 5. 408 18. 149 46. 168 1. 00 27. 38 MOTA 489 CZPHE 74 6. 640 18. 149 45. 527 1. 00 30. 18 ATOM 490 C PHE 74 3.080 21.837 44.604 5 1. 00 27. 31 **ATOM** 491 0 PHE 74 1. 912 22.034 44.951 1. 00 28. 04 **ATOM** 492 N LEU 75 3. 402 20.965 43.654 1. 00 23. 99 ATOM 493 LEU 75 2. 370 CA 20. 214 42. 958 1. 00 20. 00 ATOM 494 CB LEU 75 2. 222 20. 725 41. 534 1. 00 19. 88 **ATOM** 495 CG LEU 75 0.868 40.865 10 20. 487 1. 00 21. 27 ATOM 496 CD1 LEU 75 39. 354 1. 083 20. 282 1. 00 19. 58 ATOM 497 CD2 LEU 75 0. 190 19. 279 41. 474 1. 00 18. 85 ATOM 498 C LEU 75 2. 755 18. 758 42. 911 1. 00 18. 82 ATOM 499 0 LEU 75 3. 587 18. 369 42. 102 1.00 19.49 500 **SER 76** 43. 774 15 ATOM N 2. 143 17. 957 1. 00 21. 08 ATOM 501 CA SER 76 2. 434 16. 530 43. 834 1. 00 22. 49 ATOM 502 CB **SER 76** 2. 333 16.001 45. 261 1. 00 22. 74 MOTA 503 0G**SER 76** 2. 591 14. 612 45. 292 1. 00 20. 37 ATOM 504 C 1. 507 42.967 **SER** 76 15. 720 1. 00 23. 58 ATOM 20 505 0 SER 76 0. 309 15. 980 42. 866 1. 00 23. 06 1. 00 25. 35 ATOM 506 N LEU 77 2.064 14. 686 42. 378 ATOM 507 CA LEU 77 1. 280 13.862 41. 509 1. 00 27. 55 ATOM 508 CB LEU 77 1. 758 40.089 14. 122 1. 00 29. 38 ATOM CG LEU 77 1. 176 38. 980 509 13. 275 1. 00 32. 75 ATOM 25 510 CD1 LEU 77 -0.33413. 434 38. 974 1. 00 34. 55 ATOM CD2 LEU 77 1. 796 511 13. 695 37. 661 1. 00 32. 83 ATOM 512 C LEU 77 1. 445 12. 402 41.913 1. 00 28. 86 ATOM LEU 77 2. 527 11.826 41.760 513 0 1. 00 26. 84 ATOM 514 N ASP 78 0. 386 11. 811 42. 465 1. 00 29. 41

- 162 -ATOM ASP 78 515 CA 0. 457 10. 407 42. 865 1. 00 30. 41 **ATOM** CB ASP 78 516 -0.15010. 186 44. 255 1. 00 31. 87 ATOM 517 CG ASP 78 -0.2868.702 44. 606 1. 00 33. 99 OD1 ASP 78 ATOM 518 -1.0257. 993 43. 894 1. 00 35. 38 OD2 ASP 78 ATOM 519 0.338 45. 586 5 8. 241 1. 00 33. 31 ATOM 520 C ASP 78 -0.2709. 530 41.860 1. 00 29. 41 ATOM 521 0 **ASP** 78 -1.4849. 587 41. 732 1. 00 29. 74 ATOM 522 N LEU 79 0.472 8. 710 41. 143 1. 00 27. 93 ATOM CA 523 LEU 79 -0.16940. 184 7.858 1. 00 28. 08 10 ATOM 524CBLEU 79 0. 323 8. 173 38. 781 1. 00 25. 78 ATOM CG LEU 79 38. 371 525 1. 676 7. 627 1. 00 24. 57 ATOM 526 CD1 LEU 79 1. 845 7.871 36. 904 1. 00 25. 82 ATOM 527 CD2 LEU 79 2. 779 39. 166 8. 274 1. 00 26. 37 ATOM 528 C LEU 79 0.114 6. 420 40. 548 1. 00 31. 25 ATOM 529 0 LEU 79 1. 265 15 6.017 40.712 1. 00 32. 14 ATOM 530 N GLY 80 -0.9555. 652 40.699 1. 00 34. 99 ATOM CA 531 **GLY 80** -0.8124. 259 41.056 1. 00 38. 29 ATOM 532C **GLY 80** -2.0883. 499 40.776 1.00 40.81 ATOM 533 0 **GLY 80** -3.1003. 686 41. 452 1. 00 40. 77 ATOM 534 N 20 **GLY 81** -2.0382. 642 39.765 1. 00 43. 19 **ATOM** 535 CA **GLY 81** -3.1971.850 39. 422 1.00 45.84 ATOM 536 C **GLY 81** -3.9362. 428 38. 244 1. 00 49. 22 ATOM 537 **GLY 81** 0 -3.3282.825 37. 241 1. 00 49. 20 ATOM 38. 365 538 N THR 82 -5.2602. 465 1. 00 51. 93 ATOM 539 THR 82 25 CA -6.11737. 312 3.003 1. 00 54. 41 ATOM 540 CBTHR 82 -7.3442.090 37.060 1. 00 56. 74 ATOM 541 OG1 THR 82 -6.9080.727 36. 952 1.00 60.43 ATOM 542CG2 THR 82 -8. 043 2. 473 35. 752 1. 00 58. 23 ATOM 543 C THR 82 -6.5844. 382 37. 759 1. 00 52. 48

- 163 -ATOM 544 0 THR 82 -7.3085. 077 37. 046 1. 00 52. 21 ATOM 545 N ASN 83 -6.14838. 946 4. 778 1. 00 50. 63 **ATOM** 546 CA ASN 83 -6.5236.071 39. 466 1. 00 50. 52 ATOM 547 CBASN 83 -7.5745.911 40. 568 1. 00 53. 97 5 ATOM 548 CG ASN 83 -8.9555. 560 40.020 1. 00 58. 88 OD1 ASN 83 ATOM 549 -9.5086. 290 39. 190 1. 00 60. 51 ATOM ND2 ASN 83 550 -9.5214. 444 40. 489 1. 00 60. 30 ATOM 551 C **ASN 83** -5.3386.861 39. 997 1. 00 48. 79 ATOM 552 **0** ASN 83 -4.6826. 442 40. 956 1. 00 48. 09 ATOM N 10 553 PHE 84 -5.0688.003 39. 356 1. 00 45. 51 ATOM CA PHE 84 554 -3.9958. 907 39. 772 1. 00 40. 32 ATOM CB PHE 84 555 -2.9989. 145 38. 644 1. 00 39. 20 ATOM 556 CG PHE 84 -3.43610. 175 37. 652 1. 00 39. 52 ATOM 557 CD1 PHE 84 -4.0969.802 36. 494 1.00 40.87 ATOM 558 CD2 PHE 84 15 **-**3. 159 11. 524 37. 860 1. 00 39. 69 ATOM CE1 PHE 84 559 -4.47910. 758 35. 549 1. 00 41. 79 ATOM CE2 PHE 84 560 -3.54012. 490 36. 922 1. 00 40. 16 ATOM CZPHE 84 561 -4. 198 12. 105 35. 762 1. 00 40. 38 ATOM 562C PHE 84 -4.60410. 246 40. 176 1. 00 37. 84 **ATOM** 20 563 0 PHE 84 -5.40510.806 39. 439 1. 00 37. 11 ATOM 564 N ARG 85 -4.21610. 762 41. 338 1. 00 36. 37 ATOM 565 CA ARG 85 -4.73812. 032 41.840 1. 00 35. 14 ATOM 566 CB ARG 85 -5.49611. 779 43. 136 1.00 39.80 **ATOM** 567 ARG 85 CG -4.88810. 677 43. 970 1. 00 47. 71 **ATOM** 25 568 CD ARG 85 -5.9489. 964 44.805 1. 00 55. 73 ATOM 569 NE ARG 85 -5.3918.801 45. 493 1. 00 62. 76 ATOM CZ ARG 85 570 -4.7997. 772 44.883 1. 00 65. 65 **ATOM** NH1 ARG 85 571 -4.6847. 749 43. 557 1. 00 63. 79 ATOM NH2 ARG 85 572-4.3146. 765 45. 605 1. 00 66. 67

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	ATOM	573	C	ARG	85	-3. 664	13. 088	42. 075	1. 00 32. 14
	ATOM	574	0	ARG	85	-2. 561	12. 772	42. 522	1. 00 32. 77
	ATOM	575	N	VAL	86	-3. 977	14. 345	41. 778	1. 00 27. 45
	ATOM	576	CA	VAL	86	-2. 997	15. 405	41. 983	1. 00 26. 49
5	ATOM	577	CB	VAL	86	-2. 975	16. 400	40. 821	1. 00 24. 77
	ATOM	578	CG1	VAL	86	-3. 033	15. 655	39. 510	1. 00 26. 70
	ATOM	579	CG2	VAL	86	-4. 109	17. 373	40. 948	1. 00 24. 73
	ATOM	580	C	VAL	86	-3. 292	16. 177	43. 257	1. 00 26. 66
	ATOM	581	0	VAL	86	-4. 401	16. 121	43. 779	1. 00 28. 06
10	ATOM	582	N	MET	87	-2. 289	16. 888	43. 757	1. 00 26. 93
	ATOM	583	CA	MET	87	-2. 427	17. 677	44. 973	1. 00 25. 08
	ATOM	584	CB	MET	87	-1. 748	16. 979	46. 138	1. 00 25. 05
	ATOM	585	CG	MET	87	-1. 674	17. 833	47. 375	1. 00 24. 83
	ATOM	586	SD	MET	87	-0. 509	17. 090	48. 503	1. 00 30. 68
15	ATOM	587	CE	MET	87	-1. 544	16. 749	49. 894	1. 00 29. 41
	ATOM	588	C	MET	87	-1. 768	19. 021	44. 774	1. 00 24. 52
	ATOM	589	0	MET	87	-0. 638	19. 097	44. 298	1. 00 27. 12
	ATOM	590	N	LEU	88	-2. 455	20. 087	45. 146	1. 00 22. 16
	ATOM	591	CA	LEU	88	-1. 872	21. 398	44. 975	1. 00 20. 70
20	ATOM	592	CB	LEU	88	-2. 825	22. 309	44. 230	1. 00 20. 34
	ATOM	593	CG	LEU	88	-2. 178	23. 663	43. 991	1. 00 23. 49
	ATOM	594	CD1	LEU	88	-0. 806	23. 470	43. 354	1. 00 24. 39
	ATOM	595	CD2	LEU	88	-3. 078	24. 493	43. 094	1. 00 25. 91
	ATOM	596	C	LEU	88	-1. 535	22. 021	46. 301	1. 00 19. 94
25	ATOM	597	0	LEU	88	-2. 225	21. 794	47. 282	1. 00 21. 18
	ATOM	598	N	VAL	89	-0. 463	22. 799	46. 343	1. 00 20. 16
	ATOM	599	CA	VAL	89 .	-0. 082	23. 462	47. 580	1. 00 21. 15
	ATOM	600	CB	VAL	89	0. 984	22. 676	48. 357	1. 00 14. 95
	ATOM	601	CG1	VAL	89	1. 292	23. 385	49. 657	1. 00 7. 73

- 165 -ATOM 602 CG2 VAL 89 0. 515 21. 268 48, 609 1.00 10.59 **ATOM** 603 C **VAL 89** 0. 491 24. 829 47. 254 1. 00 27. 10 ATOM 604 0 **VAL 89** 1. 410 24. 939 46. 442 1. 00 27. 22 ATOM 605 N LYS 90 -0.06625. 866 47.875 1. 00 33. 21 ATOM 606 LYS 90 5 CA 0.401 27. 235 47.671 1. 00 40. 01 ATOM CB607 LYS 90 -0. 443 27.962 46.604 1. 00 41. 03 ATOM CG LYS 90 608 -1.94127. 979 46.850 1.00 47.19 ATOM CD 609 LYS 90 -2.74928.454 45. 622 1. 00 52. 33 ATOM 610 CE LYS 90 -4.27428. 393 45. 899 1. 00 55. 73 10 ATOM 611 NZ LYS 90 -5. 161 28. 724 1.00 56.02 44. 731 ATOM 612 C LYS 90 0. 384 28.009 48.981 1. 00 43. 61 ATOM 613 0 LYS 90 -0.57727. 943 49. 747 1.00 44.04 **ATOM** 614 N VAL 91 1. 469 28. 728 49. 241 1. 00 47. 88 **ATOM** 615 CA VAL 91 1. 587 29. 513 50. 458 1. 00 51. 82 ATOM CB15 616 VAL 91 3.059 29.780 50. 788 1. 00 51. 29 ATOM 617 CG1 VAL 91 30. 748 3. 160 51. 947 1. 00 54. 88 ATOM 618 CG2 VAL 91 3. 749 28. 479 51. 137 1. 00 48. 18 ATOM 619 C VAL 91 0.849 30. 846 50.355 1. 00 55. 01 ATOM 620 0 VAL 91 0. 994 31. 569 49. 369 1. 00 54. 57 ATOM 621 N 20 GLY 92 0.060 31. 157 51. 382 1. 00 59. 16 ATOM 622 CA GLY 92 -0.69632. 396 51.401 1. 00 64. 58 ATOM 623 C GLY 92 -0.30533. 297 52. 558 1. 00 68. 39 ATOM 624 0 GLY 92 0. 637 32. 992 53. 295 1.00 66.92 ATOM 625 N GLU 93 -1.02534. 410 52. 712 1. 00 73. 13 **ATOM** 626 25 CA **GLU 93** -0.75135. 351 53. 792 1. 00 78. 27 ATOM 627 CB GLU 93 -0.62336.780 53. 248 1.00 79.11 ATOM 628 CG GLU 93 0. 334 37. 635 54. 077 1.00 82.44 ATOM 629 CD GLU 93 0. 218 39. 120 53. 795 1.00 84.34 **ATOM** 630 0E1 GLU 93 -0. 877 39. 688 54. 018 1.00 84.71

- 166 -ATOM 631 0E2 GLU 93 1. 228 39. 718 53. 359 1. 00 85, 45 ATOM 632 C **GLU 93** -1.81335. 309 54. 904 1. 00 80. 72 ATOM 633 0 **GLU 93** -1.46935. 340 56.086 1. 00 81. 42 ATOM 634 N **GLY 94** -3.09335. 240 54. 536 1. 00 83. 03 5 ATOM 635 CA GLY 94 -4.15335. 182 55. 538 1. 00 85. 37 ATOM 636 C **GLY 94** -4.86736. 502 55. 792 1. 00 87. 51 ATOM 637 0 **GLY 94** -4.35637. 562 55. 430 1. 00 88. 65 ATOM 638 N GLU 95 -6.04136. 447 56. 427 1. 00 88. 43 ATOM 639 CA GLU 95 -6.83137. 653 56. 716 1. 00 88. 66 10 ATOM 640 CB GLU 95 -8.19237. 281 57. 328 1.00 89.61 ATOM 641 CG GLU 95 -9.07736. 406 56.448 1. 00 90. 41 ATOM 642 CDGLU 95 -8.62034. 958 56. 408 1. 00 91. 01 ATOM 0E1 GLU 95 643 34. 211 -9.08955. 523 1. 00 90. 26 ATOM 0E2 GLU 95 644 -7.80034. 565 57. 266 1.00 91.81 15 ATOM 645 C **GLU 95 -6.** 115 38. 625 57.652 1.00 88.62 ATOM 646 0 **GLU 95** -6.57639. 748 57.868 1. 00 88. 29 ATOM 647 N GLU 96 -4.99138. 182 58. 208 1.00 89.03 ATOM 648 CA **GLU 96** -4.20038. 995 59. 124 1. 00 88. 80 **ATOM** 649 CB GLU 96 -4.06538. 282 60.476 1.00 88.55 20 ATOM 650 CG **GLU 96** -5.36838. 155 61. 268 1. 00 89. 59 ATOM 651 CD **GLU 96** -6.40037. 262 60. 593 1.00 90.56 ATOM 652 0E1 GLU 96 -6.16336.040 60.481 1. 00 90. 53 ATOM 653 0E2 GLU 96 -7.45237. 785 60. 172 1.00 90.67 ATOM 654 C **GLU 96** -2.81039. 327 58. 519 1. 00 88. 40 ATOM 25 655 0 **GLU 96** -2.09740.166 59. 052 1. 00 89. 12 ATOM 656 N **GLY 97** -2.43138. 700 57. 404 1. 00 86. 87 ATOM 657 CA GLY 97 -1.13338. 917 56. 789 1. 00 85. 05 ATOM 658 C **GLY 97** -0. 161 37. 976 57. 494 1. 00 84. 17 ATOM 659 0 **GLY 97**

1. 044

38. 179

57.605

1. 00 83. 49

- 167 -ATOM 660 N GLN 98 -0. 820 36. 901 57. 977 1.00 83.07 ATOM 661 CA GLN 98 -0. 253 35. 810 58. 769 1. 00 82. 28 ATOM 662 CB GLN 98 -1.34634. 825 59. 250 1. 00 82. 41 ATOM 663 CG GLN 98 -2.64735. 462 59.699 1. 00 83. 61 ATOM 5 664 CD GLN 98 -3.74034. 427 60.007 1. 00 84. 16 ATOM 665 0E1 GLN 98 -3.60633. 239 59. 714 1. 00 84. 01 NE2 GLN 98 **ATOM** 666 -4. 905 34.685 60. 592 1. 00 84. 46 ATOM 667 C **GLN 98** 0. 735 34. 981 58. 011 1. 00 81. 85 **ATOM** 668 0 GLN 98 1. 955 35. 200 57. 956 1. 00 83. 51 10 ATOM 669 N TRP 99 0. 118 33. 962 57.470 1.00 79.05 ATOM 670 CA TRP 99 0.703 32. 914 56.706 1.00 75.85 ATOM 671 CB TRP 99 1. 993 32. 398 57. 308 1. 00 73. 88 **ATOM** 672 CG TRP 99 2.968 31. 780 56. 325 1. 00 71. 82 ATOM 673 CD2 TRP 99 3. 211 30.386 56.075 1. 00 70. 49 CE2 TRP 99 15 ATOM 674 4. 222 30. 308 55. 123 1.00 69.72 ATOM CE3 TRP 99 675 2. 671 29. 200 56. 550 1. 00 69. 52 **ATOM** CD1 TRP 99 676 3. 832 32. 464 55. 525 1. 00 71. 99 **ATOM** 677 NE1 TRP 99 4. 598 31. 589 54. 790 1. 00 71. 07 ATOM CZ2 TRP 99 678 4. 692 29. 089 54. 624 1. 00 67. 81 20 ATOM 679 CZ3 TRP 99 3. 136 27. 984 56. 080 1. 00 67. 31 ATOM 680 CH2 TRP 99 4. 151 27. 945 55. 111 1. 00 67. 77 ATOM 681 C TRP 99 -0.24731. 793 56. 673 1. 00 74. 58 ATOM 682 0 TRP 99 -1.06031. 567 57. 556 1. 00 75. 00 ATOM 683 N **SER 100** -0.09031. 087 55. 647 1. 00 72. 11 25 ATOM 684 **SER 100** CA -0.94829. 999 55. 517 1. 00 68. 48 ATOM 685 CB **SER 100** -2.37630. 466 55. 232 1. 00 68. 40 ATOM 686 0G**SER 100** -2.46731. 128 53. 985 1.00 68.76 ATOM 687 C SER 100 -0.52229. 152 54. 382 1. 00 66. 28 **ATOM** 688 0 SER 100 0. 405 29. 473 53. 632 1.00 65.13

- 168 -ATOM 689 N VAL 101 -1.22528. 028 54. 291 1. 00 64. 27 ATOM 690 CA VAL 101 -0.98227. 030 53. 262 1. 00 62. 66 ATOM 691 CB VAL 101 0.090 26. 023 53. 715 1. 00 62. 98 ATOM 692 CG1 VAL 101 1.493 26. 554 53. 459 1. 00 66. 77 **ATOM** 693 CG2 VAL 101 -0.07525. 688 55. 198 1. 00 63. 17 5 ATOM 694 C VAL 101 -2.21926. 243 52. 878 1. 00 60. 88 ATOM 695 0 VAL 101 -2.56125. 258 53. 530 1. 00 60. 62 ATOM 696 LYS 102 -2.88026. 671 N 51. 810 1. 00 58. 24 ATOM 697 CA LYS 102 -4.06625. 981 51. 337 1. 00 56. 12 ATOM 698 CBLYS 102 -4.88726.880 10 50. 410 1.00 57.06 ATOM 699 CG LYS 102 -5.88427. 806 51. 111 1. 00 60. 55 CD LYS 102 ATOM 700 -7.05627. 038 51. 748 1. 00 63. 17 ATOM 701 CE LYS 102 -8. 282 27. 944 52. 036 1.00 64.70 LYS 102 ATOM 702 NZ -8.02129. 150 52. 899 1. 00 63. 52 15 ATOM 703 C LYS 102 -3.67724. 710 50. 596 1. 00 54. 04 ATOM 704 LYS 102 -2.59924. 609 0 50.007 1. 00 52. 35 ATOM 705 N THR 103 -4.57623. 738 50. 631 1. 00 52. 24 ATOM 706 THR 103 -4.3451.00 49.72 CA 22. 474 49. 972 MOTA 707 CBTHR 103 -4.13921. 385 51.010 1. 00 49. 49 ATOM 708 OG1 THR 103 -3.39920. 316 20 50. 422 1. 00 53. 11 ATOM 709 CG2 THR 103 -5.47520. 861 51. 517 1. 00 48. 32 **ATOM** 710 C THR 103 -5. 563 22. 158 49. 106 1.00 49.61 THR 103 -6.693ATOM 711 0 22. 435 49. 507 1. 00 50. 24 ATOM 712 N LYS 104 -5.33021. 587 47. 924 1. 00 48. 56 ATOM 713 CA LYS 104 -6.40421. 251 46. 983 25 1. 00 48. 50 ATOM CB LYS 104 -6.46922. 298 714 45. 864 1. 00 49. 98 ATOM 715 CG LYS 104 -6.75323. 737 46. 313 1. 00 56. 05 LYS 104 ATOM 716 CD-8.19523. 932 46. 814 1. 00 60. 38 ATOM 717 CE LYS 104 -8.45625. 383 47. 254 1. 00 62. 32

- 169 -ATOM 718 NZ LYS 104 -9.84525. 649 47. 761 1. 00 61. 31 ATOM 719 C LYS 104 -6.22419. 878 46. 332 1. 00 48. 13 ATOM 720 0 LYS 104 -5.28619. 685 45. 563 1. 00 49. 60 ATOM 721 N HIS 105 -7.12718. 936 46. 606 1. 00 47. 57 5 ATOM 722 CA HIS 105 -7.02317. 601 46.010 1.00 47.23 ATOM 723 CB HIS 105 -7. 165 16. 529 47. 074 1. 00 47. 40 ATOM 724 CG HIS 105 -6.24116. 709 48. 228 1. 00 49. 37 ATOM 725 CD2 HIS 105 -5.09816.066 48. 563 1. 00 49. 55 ATOM 726 ND1 HIS 105 -6.45917.648 49. 212 1. 00 50. 43 10 ATOM 727CE1 HIS 105 -5.49317. 571 50. 110 1.00 51.38 ATOM 728 NE2 HIS 105 -4.65516.619 49.740 1.00 50.58 ATOM 729 C HIS 105 -8.0301.00 46.39 17. 304 44. 907 730 ATOM 0 HIS 105 -9.19517. 692 44. 985 1. 00 49. 62 ATOM 731 N **GLN 106** -7.57516. 580 43. 894 1. 00 42. 98 ATOM 732 CA **GLN 106** 15 -8. 419 16. 226 42. 771 1. 00 40. 44 ATOM 733 CBGLN 106 -8. 284 17. 285 41. 685 1. 00 40. 41 ATOM 734 CG **GLN 106** -9.54617. 548 40. 908 1. 00 40. 59 GLN 106 ATOM 735 CD -10.42816. 324 40.813 1. 00 40. 54 ATOM OE1 GLN 106 736 -11.06115. 927 41. 795 1. 00 39. 16 ATOM 20 737 NE2 GLN 106 -10.47515. 712 39. 631 1. 00 40. 06 **ATOM** 738 C **GLN 106** -7.94014. 878 42. 249 1. 00 40. 70 ATOM 739 0 GLN 106 -6.74514.699 42.012 1.00 41.69 ATOM 740 N MET 107 -8.86713. 937 42.066 1.00 41.01 ATOM 741 CA MET 107 -8.53212. 588 41. 599 1. 00 40. 17 25 ATOM 742 CB MET 107 -9.08311. 551 42. 588 1. 00 42. 07 ATOM 743 CG MET 107 -8.77210.094 42. 249 1.00 44.67 ATOM 744 SD 9. 202 MET 107 -10.18541.551 1. 00 50. 71 ATOM 745 CE MET 107 -10.6888.056 42. 927 1. 00 43. 37 **ATOM** 746 C MET 107 -9. 059 12. 294 40. 204 1. 00 38. 93

- 170 -**ATOM** 747 0 MET 107 -10. 264 12. 285 39. 979 1.00 41.30 ATOM 748 N TYR 108 -8.16112. 044 39. 264 1.00 37.96 ATOM TYR 108 -8.58811. 750 749 CA 37. 907 1. 00 38. 48 **ATOM** 750 CBTYR 108 -7. 670 12. 454 36.900 1.00 35.63 ATOM 751 CG TYR 108 -7.73213. 972 36. 977 1. 00 35. 18 5 ATOM 752 CD1 TYR 108 -7.49214.645 38. 180 1.00 37.21 ATOM 753 CE1 TYR 108 -7.55016.047 38. 268 1.00 34.81 ATOM 754 CD2 TYR 108 -8.03114. 735 35. 857 1. 00 34. 14 ATOM CE2 TYR 108 -8.092755 16. 134 35. 931 1.00 35.09 CZ**ATOM** 756 TYR 108 -7.85216. 783 37. 139 1. 00 35. 25 10 **ATOM** OH TYR 108 -7.93718. 158 1.00 33.27 757 37. 211 758 C TYR 108 -8.58310. 241 ATOM 37. 689 1. 00 40. 17 759 TYR 108 -7.817ATOM 0 9. 514 38. 325 1. 00 38. 04 ATOM 760 N SER 109 -9.4699.765 36. 818 1. 00 42. 63 ATOM 761 CA SER 109 -9.5248.341 36. 530 1.00 44.60 15 ATOM 762 CB SER 109 -10.9297. 787 36. 736 1. 00 43. 05 0G -10.9266.385 ATOM 763 SER 109 36. 522 1.00 41.66 -9.090ATOM 764 C SER 109 8. 106 35. 097 1. 00 46. 74 ATOM 765 0 SER 109 -9. 531 8. 799 34. 182 1. 00 44. 65 ATOM 766 N ILE 110 -8. 217 7. 120 20 34. 918 1. 00 50. 31 **ATOM** CA ILE 110 -7.6866.782 767 33. 608 1. 00 55. 29 ATOM ILE 110 -6.3266.060 768 CB 33. 731 1. 00 54. 32 ATOM 769 CG2 ILE 110 -5.6905. 932 32. 364 1. 00 56. 16 ATOM 770 CG1 ILE 110 -5. 373 6.844 34. 626 1. 00 53. 30 **ATOM** CD1 ILE 110 -4.06725 771 6. 117 34. 869 1. 00 51. 57 ATOM 772 C ILE 110 -8.6215. 882 32. 799 1. 00 59. 70 ATOM ILE 110 -8.906773 0 4. 749 33. 199 1. 00 58. 82

ATOM

ATOM

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CD

PRO 111

PRO 111

-9. 114

-8.972

6. 381

7. 759

31.650

31. 142

1.00 64.10

1. 00 64. 05

- 171 -ATOM 776 CA PRO 111 -10.0125. 608 30. 788 1. 00 68. 40 ATOM 777 CB PRO 111 -10.1186. 484 29. 547 1. 00 67. 29 -10. 105 ATOM 778 CG PRO 111 7.860 30. 144 1. 00 63. 88 ATOM 779 C PRO 111 -9.4164. 231 30. 494 1. 00 72. 88 5 ATOM 780 0 PRO 111 -8.1954.065 30. 506 1. 00 73. 72 **ATOM** 781 N GLU 112 -10.2803. 250 30. 239 1. 00 77. 60 ATOM 782 CA GLU 112 -9.8451.879 29. 958 1. 00 80. 79 ATOM 783 CB GLU 112 -11.0720.968 29. 798 1. 00 82. 29 ATOM 784 CG GLU 112 -10.748-0.49829. 524 1. 00 83. 62 10 ATOM 785 CD GLU 112 -1.24728.851 -11.8961. 00 85. 04 ATOM 786 0E1 GLU 112 -11. 697 -2.42328. 470 1.00 85.60 ATOM 787 0E2 GLU 112 -12.995-0.66528. 700 1. 00 85. 42 ATOM 788 C GLU 112 -8.9711. 806 28. 702 1. 00 82. 21 **ATOM** 789 0 GLU 112 -7.9361. 137 28. 693 1. 00 82. 17 ATOM 790 N ASP 113 2.501 15 -9.39427. 649 1. 00 83. 97 **ATOM** 791 CA ASP 113 -8.6602. 522 26. 385 1. 00 85. 79 ATOM 792 CBASP 113 -9.5063. 221 25. 302 1. 00 86. 45 793 ASP 113 ATOM CG -9.9614. 624 25. 712 1. 00 87. 32 OD1 ASP 113 ATOM 794 -10.6554. 756 26. 748 1. 00 86. 75 ATOM 795 OD2 ASP 113 -9.62920 5. 595 24. 991 1. 00 87. 18 ATOM 796 C ASP 113 -7.2973. 215 26. 533 1. 00 86. 44 797 ATOM 0 ASP 113 -6.4673. 195 25. 617 1. 00 86. 35 ATOM 798 N ALA 114 -7.0753.813 27. 701 1. 00 86. 34 ATOM CA -5.837799 ALA 114 4. 533 28.000 1. 00 85. 22 25 ATOM 800 CB ALA 114 -6.1745. 904 28. 585 1. 00 84. 46 ATOM 801 C ALA 114 -4.9283. 768 28. 963 1. 00 83. 67 ATOM 802 0 ALA 114 -3.7163.692 28. 762 1. 00 83. 48 ATOM 803 N MET 115 -5.5283. 212 30. 012 1. 00 81. 79 ATOM 804 CA -4.802MET 115 2. 457 31. 023 1. 00 78. 70

- 172 -ATOM 805 CBMET 115 -5. 776 2. 050 32. 135 1.00 81.16 ATOM 806 CG MET 115 -5. 148 1.863 33. 503 1. 00 84. 52 ATOM 807 SD MET 115 -3.9780.492 33. 553 1. 00 90. 44 **ATOM** 808 CE MET 115 -5.060 -0.89134. 119 1. 00 88. 49 **ATOM** 809 C 5 MET 115 -4.1451. 224 30. 391 1. 00 76. 27 ATOM 810 0 MET 115 -3.0660.809 30. 813 1. 00 74. 47 ATOM 811 N THR 116 -4.7960.658 29. 372 1.00 74.50 ATOM 812 CA THR 116 -4.282-0.51828. 666 1. 00 72. 46 ATOM . CB 813 THR 116 -5.399-1.52428. 309 1. 00 72. 22 10 ATOM 814 OG1 THR 116 -6.200-0.99327. 244 1. 00 71. 17 CG2 THR 116 ATOM 815 -6.275-1.80529. 516 1.00 71.94 ATOM 816 С THR 116 -3.621-0. 110 27. 356 1. 00 71. 75 ATOM 817 0 THR 116 -3.562-0.89926. 412 1.00 71.39 ATOM 818 N **GLY 117** -3.1421. 131 27. 301 1.00 71.09 15 ATOM 819 CA GLY 117 -2.4771.639 26. 110 1. 00 68. 62 **ATOM** 820 C GLY 117 -0.96126. 260 1. 651 1. 00 66. 70 ATOM 821 0 GLY 117 -0.384 0.702 26. 798 1. 00 67. 20 ATOM 822 N THR 118 -0. 313 2. 716 25. 783 1. 00 63. 05 ATOM 823 CA THR 118 1. 142 2. 844 25. 876 1. 00 59. 92 20 ATOM 824 CB THR 118 1.796 3. 020 24. 502 1. 00 59. 06 **ATOM** 825 OG1 THR 118 1.013 3.926 23. 718 1. 00 57. 88 ATOM 826 CG2 THR 118 1. 917 1.688 23. 794 1. 00 59. 21 ATOM 827 C THR 118 1. 548 4. 038 26. 721 1. 00 58. 97 ATOM 828 0 THR 118 0.764 4. 971 26. 912 1. 00 58. 11 829 25 ATOM N **ALA 119** 2. 782 4.001 27. 218 1. 00 56. 72 ATOM 830 CA ALA 119 3. 313 5.071 28. 052 1. 00 52. 86 ATOM 831 CB ALA 119 4. 807 4. 938 28. 177 1. 00 51. 30 ATOM 832 C ALA 119 2. 972 6.399 27. 421 1. 00 51. 58 ATOM 833 0 ALA 119 2. 456 7. 301 28. 080 1. 00 52. 70

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	ATOM	834	N	GLU	120	3. 260		26. 131	1. 00 48	8. 02
	ATOM	835	CA	GLU	120	2. 994		25. 386	1. 00 40	
	ATOM	836	СВ	GLU	120	3. 194		23. 894	1. 00 49	
	ATOM	837	CG		120	4. 210	6. 381	23. 550	1. 00 5	
5	ATOM	838	CD		120	5. 630	6. 736	23. 945	1. 00 53	
	ATOM	839	0E1	GLU	120	5. 962	6. 621	25. 141	1. 00 58	
	ATOM	840		GLU		6. 411	7. 139	23. 057	1. 00 52	
	ATOM	841	С		120	1. 557	8. 140	25. 630	1. 00 44	
	ATOM	842	0		120	1. 295	9. 257	26. 070	1. 00 44	
10	ATOM	843	N		121	0. 627	7. 235	25. 351	1. 00 41	
	ATOM	844	CA	MET	121	-0. 791	7. 525	25. 513	1. 00 38	
	ATOM	845	CB	MET	121	-1. 626	6. 358	24. 990	1. 00 41	l. 30
	ATOM	846	CG	MET	121	-1. 721	6. 328	23. 479	1. 00 46	3. 24
	ATOM	847	SD	MET	121	-2. 483	4. 835	22. 838	1. 00 50). 88
15	ATOM	848	CE	MET	121	-3. 908	4. 669	23. 961	1. 00 50). 02
	ATOM	849	C	MET	121	-1. 190	7. 820	26. 937	1. 00 34	l. 60
	ATOM	850	0	MET	121	-1. 910	8. 780	27. 204	1. 00 31	. 69
	ATOM	851	N	LEU	122	-0. 719	6. 985	27. 852	1. 00 32	. 63
	ATOM	852	CA	LEU	122	-1. 051	7. 141	29. 263	1. 00 30	. 24
20	ATOM	853	CB	LEU	122	-0. 256	6. 140	30. 108	1. 00 27	. 33
	ATOM	854	CG	LEU	122	-0. 778	5. 923	31. 533	1. 00 21	. 99
	ATOM	855	CD1	LEU	122	-0. 279	4. 601	32. 031	1. 00 22	. 53
	ATOM	856	CD2	LEU	122	-0. 366	7. 034	32. 456	1. 00 17	. 78
	ATOM	857	C	LEU	122	-0. 759	8. 551	29. 746	1. 00 28	. 67
25	ATOM	858	0	LEU	122	-1. 619	9. 228	30. 326	1. 00 25	. 21
	ATOM	859	N	PHE	123	0. 469	8. 987	29. 502	1. 00 26	. 83
	ATOM	860	CA	PHE	123	0. 871	10. 306	29. 929	1. 00 25	. 29
	ATOM	861	CB	PHE	123	2. 387	10. 398	29. 908	1. 00 20	. 22
	ATOM	862	CG	PHE	123	3. 015	9. 772	31. 112	1. 00 15	. 51

- 174 -ATOM 863 CD1 PHE 123 3. 538 8. 494 31. 064 1. 00 12. 96 **ATOM** CD2 PHE 123 864 3. 028 10. 457 32. 328 1. 00 13. 35 CE1 PHE 123 **ATOM** 865 4.067 7.910 32. 217 1. 00 12. 87 **ATOM** CE2 PHE 123 866 3. 552 9.879 33. 484 1.00 9.69 5 ATOM 867 CZPHE 123 4.072 8. 609 33. 432 1.00 9.56 ATOM 868 C PHE 123 0. 202 11. 432 29. 157 1. 00 26. 20 ATOM 869 0 PHE 123 -0.10212. 489 29. 722 1. 00 26. 61 ATOM 870 N ASP 124 -0.05311. 207 27. 875 1. 00 24. 47 ATOM 871 ASP 124 CA -0.75012. 210 27. 090 1. 00 23. 14 ATOM 872 ASP 124 10 CB -1.22811.614 25. 785 1. 00 24. 52 ATOM 873 ASP 124 CG -0.17824. 747 11. 628 1. 00 27. 01 ATOM 874 OD1 ASP 124 -0.37610. 955 23. 715 1.00 26.39 ATOM OD2 ASP 124 875 0.839 12. 325 24. 968 1. 00 29. 23 ATOM 876 C ASP 124 -1.96712.650 27. 875 1. 00 21. 89 15 ATOM 877 0 ASP 124 -2.36113. 815 27. 841 1. 00 20. 01 ATOM 878 N TYR 125 -2.56211.688 28. 574 1. 00 20. 84 ATOM 879 CA TYR 125 -3.74911. 943 29. 371 1. 00 20. 51 ATOM 880 CBTYR 125 -4. 414 10. 619 29. 792 1. 00 20. 43 ATOM 881 CG TYR 125 -5.79610.794 30. 394 1. 00 22. 84 **ATOM** 20 882 CD1 TYR 125 -6.08310.358 31. 692 1. 00 23. 51 ATOM 883 CE1 TYR 125 -7.34510. 584 32. 268 1. 00 31. 08 ATOM 884 CD2 TYR 125 -6.80311. 451 29.678 1. 00 26. 43 ATOM 885 CE2 TYR 125 -8. 064 11. 685 30. 232 1. 00 31. 61 ATOM 886 CZ TYR 125 -8. 336 11. 255 31. 528 1. 00 34. 64 ATOM 25 887 OH TYR 125 -9.58511. 520 32. 073 1. 00 38. 10 ATOM 888 C TYR 125 -3.38212. 752 30.605 1. 00 19. 11 ATOM 889 0 TYR 125 -3. 904 13. 848 30. 824 1. 00 16. 08 ATOM 890 N ILE 126 -2.46512. 212 31. 399 1. 00 17. 91 ATOM 891 CA ILE 126 -2.04912. 879 32. 615 1. 00 17. 82

- 175 -ATOM 892 CB ILE 126 -0.81912. 236 33. 203 1. 00 19. 82 ATOM 893 CG2 ILE 126 -0.48912. 905 34. 538 1. 00 18. 77 ATOM 894 CG1 ILE 126 -1.05510. 732 33. 331 1. 00 21. 27 ATOM 895 CD1 ILE 126 0.045 9. 984 34. 062 1. 00 23. 92 5 ATOM 896 C ILE 126 -1.71714. 313 32. 325 1.00 18.09 ATOM 897 0 ILE 126 -1.99115. 205 33. 123 1.00 16.68 ATOM 898 N SER 127 -1.10814. 532 31. 172 1.00 19.12 ATOM 899 CA SER 127 -0.74715. 877 30. 789 1. 00 20. 96 ATOM 900 CB SER 127 -0.05715. 857 29. 432 1.00 19.89 ATOM 901 0G SER 127 10 0.569 17. 100 29. 190 1. 00 22. 20 ATOM 902 C SER 127 -2. 011 16. 742 30. 746 1.00 21.92 ATOM 903 0 SER 127 -2.17717.658 31. 551 1. 00 20. 25 904 **ATOM** N **GLU 128** -2.90216. 431 29. 813 1. 00 23. 87 ATOM 905 CA GLU 128 **-4**. 152 17. 161 29. 670 1. 00 26. 98 15 ATOM 906 CB GLU 128 -5. 111 16. 353 28. 802 1. 00 33. 10 ATOM 907 CG GLU 128 -6.47116.990 28. 544 1. 00 39. 51 ATOM CD 908 GLU 128 -7. 280 1. 00 44. 52 16. 175 27. 544 ATOM 909 OE1 GLU 128 -7. 211 16. 481 26. 327 1. 00 46. 11 0E2 GLU 128 ATOM 910 -7. 963 15. 218 27. 980 1. 00 43. 93 20 ATOM 911 C **GLU 128** -4.79717. 431 31. 020 1. 00 26. 55 912 ATOM 0 GLU 128 -5.17718. 561 31. 334 1. 00 26. 16 ATOM 913 N CYS 129 -4.92916. 384 31. 820 1. 00 26. 36 ATOM 914 CA CYS 129 -5.53216. 535 33. 130 1. 00 26. 47 ATOM 915 CB CYS 129 -5.45215. 219 33. 893 1. 00 28. 39 25 ATOM CYS 129 916 SG -6.45013. 922 33. 126 1. 00 37. 58 ATOM 917 C CYS 129 -4.85333. 914 17. 636 1. 00 25. 00 ATOM 918 0 CYS 129 -5.51518. 561 34. 372 1. 00 24. 97 **ATOM** 919 N ILE 130 -3.53217. 536 1.00 24.74 34.059 **ATOM** 920 CAILE 130 -2.76318. 536 34. 793 1. 00 21. 55

- 176 -ATOM 921 CB ILE 130 -1.24518. 255 34. 709 1. 00 17. 55 ATOM 922 CG2 ILE 130 -0.45819. 404 35. 304 1. 00 15. 00 ATOM 923 CG1 ILE 130 -0.91516. 984 35. 490 1. 00 16. 42 ATOM 924 CD1 ILE 130 0. 574 16. 713 35. 623 1. 00 18. 34 5 ATOM 925 C ILE 130 -3.07019. 910 34. 219 1.00 23.54 ATOM 926 0 ILE 130 -3.57220. 780 34. 926 1. 00 21. 27 ATOM 927 N SER 131 -2.78520. 091 32. 933 1. 00 26. 25 ATOM 928 CA SER 131 -3.04821. 353 32. 270 1. 00 28. 50 ATOM 929 CB SER 131 -3.01121. 186 30. 764 1. 00 28. 76 10 ATOM 930 0G SER 131 -3.85622. 154 30. 164 1. 00 32. 87 ATOM SER 131 931 C -4. 417 21. 851 32.661 1. 00 31. 48 ATOM 932 0 SER 131 -4.58623. 002 33. 057 1. 00 33. 67 ATOM 933 N ASP 132 -5. 411 20. 986 32. 546 1. 00 34. 56 ATOM 934 CA ASP 132 -6.75321. 397 32. 908 1.00 39.04 ATOM 15 935 CB ASP 132 -7. 735 20. 248 32.694 1. 00 44. 84 ATOM 936 CG ASP 132 -9.16520.650 32. 987 1. 00 50. 51 ATOM 937 OD1 ASP 132 -9.76421. 347 32. 131 1. 00 53. 56 ATOM 938 OD2 ASP 132 -9.67420. 283 34.078 1. 00 52. 37 ATOM 939 C ASP 132 -6.79021. 843 34. 376 1. 00 38. 23 ATOM 20 940 0 ASP 132 -7.16022. 982 34. 677 1. 00 36. 81 ATOM 941 N PHE 133 -6.39420. 932 35. 270 1. 00 36. 88 ATOM 942 CA PHE 133 -6.37221. 170 36. 713 1.00 34.85 ATOM 943 CB PHE 133 -5.60420.060 37. 433 1. 00 33. 59 **ATOM** 944 PHE 133 CG -5. 343 20. 362 38. 878 1. 00 34. 77 25 ATOM 945 CD1 PHE 133 -6.39620. 547 39.760 1. 00 35. 58 ATOM 946 CD2 PHE 133 -4.04320. 523 39. 348 1. 00 37. 81 **ATOM** 947 CE1 PHE 133 -6.15920.896 41.091 1.00 37.66 **ATOM** 948 CE2 PHE 133 -3. 792 20. 872 40. 678 1. 00 38. 00 ATOM 949 CZ PHE 133 -4.85021. 059 41. 548 1. 00 38. 85

- 177 -ATOM 950 C PHE 133 -5. 755 22. 503 37. 094 1. 00 34. 28 **ATOM** 951 0 PHE 133 -6.27423. 226 37. 947 1. 00 33. 97 **ATOM** 952 N LEU 134 -4.62222. 813 36. 482 1. 00 33. 97 ATOM 953 CA LEU 134 -3.95824. 070 36.766 1. 00 31. 79 5 ATOM 954 CB LEU 134 -2.59024. 109 36.089 1. 00 24. 12 ATOM 955 CG LEU 134 -1.61823. 026 36. 545 1. 00 16. 64 ATOM 956 CD1 LEU 134 -0.36823. 101 35. 705 1. 00 15. 98 CD2 LEU 134 **ATOM** 957 -1.30523. 184 38. 014 1. 00 10. 77 ATOM 958 C LEU 134 -4. 855 25. 176 36. 234 1.00 34.44 10 ATOM 959 0 LEU 134 -5. 111 26. 163 36. 920 1.00 34.41 ATOM 960 N ASP 135 · -5. 365 24. 999 35. 022 1. 00 37. 26 ATOM 961 CA ASP 135 -6.23026. 014 34. 454 1. 00 42. 65 ATOM 962 CB ASP 135 -6.81525. 565 33. 121 1. 00 46. 76 ATOM 963 CG ASP 135 -7. 707 26.629 32. 509 1. 00 52. 18 ATOM 15 964 OD1 ASP 135 -8.65926. 271 31. 772 1. 00 53. 75 ATOM OD2 ASP 135 965 -7. 443 27. 829 32. 772 1. 00 52. 70 ATOM 966 C ASP 135 -7.38626. 381 35. 383 1.00 43.96 ATOM ASP 135 967 0 -7.64327. 563 35. 619 1. 00 44. 98 ATOM 968 LYS 136 N -8.08425. 368 35. 894 1. 00 44. 30 20 ATOM 969 CA LYS 136 -9.22525. 578 36. 780 1.00 44.56 ATOM 970 CB LYS 136 -9.88924. 237 37. 124 1. 00 46. 76 ATOM 971 CG LYS 136 -11. 195 24. 350 37. 941 1.00 52.67 ATOM 972 LYS 136 CD -11.91022. 981 38. 128 1. 00 55. 98 ATOM 973 CE LYS 136 -13.36723. 120 38. 628 1. 00 55. 25 25 ATOM 974 NZ LYS 136 -14.10621. 817 38. 719 1. 00 51. 28 ATOM 975 C LYS 136 -8.86226. 306 38. 069 1.00 44.85 ATOM 976 0 LYS 136 -9.73026. 894 38. 717 1. 00 45. 87 ATOM 977 N HIS 137 -7.58626. 273 38. 444 1. 00 44. 25 ATOM HIS 137 978 CA -7. 149 ´ 26. 937 39. 670 1. 00 43. 21

- 178 -ATOM 979 CB HIS 137 -6. 434 25. 937 40. 585 1. 00 44. 13 ATOM 980 CG HIS 137 -7.34424. 915 41. 199 1. 00 45. 24 ATOM CD2 HIS 137 981 -7. 676 24. 680 42. 492 1.00 45.35 **ATOM** ND1 HIS 137 982 -8.04223. 991 40. 452 1.00 45.45 **ATOM** 983 **CE1 HIS 137** -8.76423. 231 5 41. 257 1. 00 45. 40 NE2 HIS 137 ATOM 984 -8.56023.629 42.500 1. 00 44. 34 ATOM C HIS 137 -6.24228. 132 985 39.400 1.00 41.96 ATOM 986 0 HIS 137 -5.59228. 649 40. 307 1.00 40.24 ATOM 987 N **GLN 138** -6.21728. 577 38. 151 1. 00 42. 87 10 ATOM 988 CA GLN 138 -5.39029. 706 37. 766 1.00 44.93 **ATOM** 989 CB**GLN 138** -5.94930. 993 38. 373 1.00 47.58 **ATOM** 990 GLN 138 CG -7.25831. 448 37. 749 1.00 51.96 ATOM 991 CD GLN 138 -7.41632. 966 37. 766 1. 00 55. 20 **ATOM** 992 0E1 GLN 138 -6.68033.698 37.088 1.00 56.05 15 **ATOM** 993 NE2 GLN 138 -8. 375 33. 445 38. 546 1. 00 55. 44 ATOM 994 C GLN 138 -3.92129. 537 38. 162 1. 00 44. 67 **ATOM** 995 0 GLN 138 -3.31630. 437 38. 747 1. 00 45. 78 **ATOM** 996 N -3.350MET 139 28. 383 37. 836 1. 00 41. 86 ATOM 997 CA MET 139 -1.95128. 109 38. 138 1.00 38.60 20 ATOM 998 CB MET 139 -1.84627. 062 39. 236 1. 00 39. 19 ATOM 999 CG MET 139 -2.04827.660 40.604 1.00 41.24 1000 ATOM SD MET 139 -0.85928. 992 40. 852 1.00 47.65 ATOM 1001 CE MET 139 0.308 28. 217 42.007 1.00 44.32 ATOM 1002 C -1.232MET 139 27. 653 36. 881 1. 00 36. 60 25 **ATOM** 1003 0 MET 139 -0.31626. 823 36. 910 1. 00 35. 29 **ATOM** 1004 N LYS 140 -1.65928. 237 35. 771 1.00 34.23 ATOM 1005 CA LYS 140 -1. 101 27. 921 34. 477 1. 00 32. 15 ATOM 1006 CB LYS 140 -2.19828.062 33. 417 1.00 31.04 **ATOM** 1007 CG LYS 140 27. 293 -1.97032. 116 1. 00 31. 48

- 179 -ATOM -2. 184 25. 780 32. 275 1008 CD LYS 140 1. 00 32. 43 ATOM LYS 140 1009 CE -2. 112 25. 015 30. 925 1.00 30.89 ATOM NZ LYS 140 -0.811 25. 130 30. 168 1.00 29.56 1010 ATOM LYS 140 0.085 1011 C 28. 834 34. 161 1. 00 31. 02 5 ATOM 1012 0 LYS 140 0. 047 30. 045 34. 412 1. 00 29. 99 ATOM HIS 141 1. 143 28. 228 33. 627 1. 00 31. 35 1013 N ATOM HIS 141 2. 353 28. 940 33. 244 1. 00 30. 03 1014 CA ATOM 1015 CB HIS 141 1. 989 30. 145 32. 385 1. 00 30. 05 31. 305 ATOM HIS 141 1.001 29. 836 1016 CG 1. 00 31. 15 ATOM CD2 HIS 141 -0. 132 10 1017 30. 473 30. 927 1.00 30.91 **ATOM** ND1 HIS 141 1018 1. 148 28. 769 30. 448 1. 00 33. 49 ATOM 1019 CE1 HIS 141 0. 147 28. 763 29. 584 1. 00 35. 03 ATOM NE2 HIS 141 -0. 643 1020 29. 787 29. 853 1. 00 32. 67 ATOM C HIS 141 1021 3. 138 29. 396 34. 460 1. 00 29. 17 ATOM 1022 0 HIS 141 4. 211 15 29. 983 34. 341 1. 00 28. 17 LYS 142 ATOM 1023 N 2.601 29. 108 35. 635 1. 00 28. 81 ATOM 1024 CA LYS 142 3. 248 29. 505 36. 869 1. 00 29. 17 ATOM 1025 CB LYS 142 2. 317 29. 240 38. 065 1. 00 33. 65 ATOM 1026 LYS 142 0.986 38. 072 CG 30. 042 1. 00 39. 35 20 ATOM 1027 CDLYS 142 1. 194 31. 561 38. 214 1. 00 42. 74 ATOM CE LYS 142 1028 -0. 122 32. 360 38. 170 1. 00 45. 49 ATOM 1029 NZ LYS 142 0. 110 33. 844 38. 325 1.00 46.19 ATOM 1030 C LYS 142 4. 575 28. 785 37. 075 1. 00 26. 49 ATOM 1031 0 LYS 142 5. 340 29. 138 37.966 1. 00 26. 10 4.862 ATOM 1032 N LYS 143 27. 784 36. 254 25 1. 00 24. 58 ATOM 1033 CA LYS 143 6. 106 27. 042 36. 416 1. 00 22. 67 ATOM 7. 258 1034 CB LYS 143 27. 847 35. 836 1. 00 21. 51 ATOM CG LYS 143 8. 533 27. 071 35. 737 1035 1. 00 22. 59 ATOM 1036 CDLYS 143 9. 319 27. 510 34. 516 1.00 25.81

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- 180 -**ATOM** 1037 CE LYS 143 10. 455 26. 542 34. 240 1. 00 28. 01 32. 959 1. 00 27. 25 **ATOM** LYS 143 11. 140 26. 828 1038 NZ 26. 732 37. 896 1. 00 22. 14 ATOM C LYS 143 6. 383 1039 27.459 38. 556 1. 00 21. 99 ATOM 1040 0 LYS 143 7. 133 5. 766 25.655 38. 401 1. 00 20. 81 ATOM LEU 144 5 1041 N ATOM 1042 CA LEU 144 5.910 25. 214 39. 797 1.00 16.90 **ATOM** 1043 CBLEU 144 4. 577 25. 351 40. 567 1. 00 16. 78 3. 208 24. 956 39. 983 1. 00 18. 43 ATOM 1044 CG LEU 144 CD1 LEU 144 2. 148 24. 915 41.074 1.00 17.60 ATOM 1045 CD2 LEU 144 2.795 25.960 38. 929 1.00 19.20 ATOM 1046 10 ATOM LEU 144 6.432 23. 781 39. 933 1. 00 15. 80 1047 C LEU 144 6. 265 22. 958 39. 032 1. 00 12. 24 ATOM 1048 0 23. 478 41.076 1. 00 16. 26 **ATOM** 1049 N PRO 145 7. 078 1.00 15.64 **ATOM** 1050 PRO 145 7. 227 24. 446 42. 172 CD 7.678 22. 196 41.467 1. 00 14. 17 15 **ATOM** 1051 CA PRO 145 8.079 22. 427 42. 923 1. 00 18. 10 ATOM 1052 CB PRO 145 8.378 23.860 42.963 1.00 17.14 ATOM 1053 CG PRO 145 6.707 1. 00 12. 75 1054 C PRO 145 21.050 41. 357 ATOM 1055 5. 580 21. 141 41.852 1. 00 12. 27 ATOM 0 PRO 145 1056 7. 160 19. 957 40. 758 1. 00 10. 29 ATOM N LEU 146 20 6.290 18.804 40.560 1. 00 11. 21 ATOM 1057 CA LEU 146 6.156 18. 539 1.00 7.24 ATOM 1058 CB LEU 146 39. 075 1059 CG LEU 146 5. 160 17. 439 38. 824 1.00 3.01 ATOM 3.817 17. 832 39. 389 1.00 1.00 ATOM 1060 CD1 LEU 146 17. 215 1.00 3.06 25 ATOM 1061 CD2 LEU 146 5. 083 37. 342 6.696 17. 502 41. 233 1. 00 12. 36 ATOM 1062 C LEU 146 ATOM 1063 0 LEU 146 7.629 16.851 40.790 1. 00 15. 11 5. 972 17. 086 42. 262 1. 00 14. 72 ATOM 1064 N GLY 147 GLY 147 6. 333 15. 851 42. 937 1.00 17.81 ATOM 1065 CA

- 181 -ATOM 1066 C **GLY 147** 5. 716 14. 586 42. 371 1. 00 18. 51 ATOM 1067 0 GLY 147 4. 689 14. 644 41.704 1. 00 20. 85 ATOM 1068 N PHE 148 6. 342 13. 440 42.631 1. 00 19. 28 ATOM 1069 CA PHE 148 5.825 12. 167 42. 142 1. 00 20. 55 ATOM 1070 CB PHE 148 6.707 11.635 5 41.023 1. 00 16. 36 **ATOM** 1071 CG PHE 148 6.593 12. 409 39.759 1. 00 17. 72 **ATOM** 1072 CD1 PHE 148 6. 792 13. 779 39. 753 1. 00 17. 99 CD2 PHE 148 6. 298 ATOM 1073 11. 769 38. 560 1. 00 21. 10 CE1 PHE 148 **ATOM** 1074 6.695 14. 509 38. 570 1. 00 22. 37 **ATOM** CE2 PHE 148 1075 6. 198 12. 494 37. 362 1. 00 22. 82 10 **ATOM** 1076 CZPHE 148 6.398 13.864 37. 366 1. 00 21. 67 PHE 148 ATOM 1077 C 5. 712 1. 00 22. 75 11. 104 43. 222 6.691 ATOM 1078 0 PHE 148 10. 783 43. 885 1.00 24.66 **ATOM** 1079 N THR 149 4. 513 10. 562 43. 403 1. 00 24. 45 **ATOM** 1080 CA THR 149 4. 312 9. 514 15 44. 387 1. 00 24. 75 **ATOM** 1081 CB THR 149 3. 365 9. 917 45. 497 1. 00 23. 76 1082 ATOM OG1 THR 149 2. 757 11. 175 45. 192 1. 00 25. 51 1083 CG2 THR 149 9.989 **ATOM** 4. 107 46. 786 1. 00 22. 63 ATOM 1084 C THR 149 3.705 8. 306 43.715 1. 00 27. 38 **ATOM** 1085 THR 149 0 3. 093 8. 405 42. 647 1. 00 24. 58 20 1086 PHE 150 ATOM N 3.857 7. 160 44. 361 1. 00 30. 07 **ATOM** 1087 CA PHE 150 3. 327 5. 936 43.811 1.00 32.54 ATOM 1088 CB PHE 150 4. 455 5. 120 43. 215 1. 00 29. 97 ATOM 1089 CG PHE 150 5. 172 5. 820 42. 119 1. 00 27. 55 ATOM 1090 CD1 PHE 150 6. 134 6.770 25 42. 397 1. 00 27. 41 CD2 PHE 150 ATOM 1091 4.850 5. 561 40. 798 1. 00 27. 56 ATOM CE1 PHE 150 6.770 1092 7. 447 41.366 1. 00 28. 61 ATOM CE2 PHE 150 1093 5. 481 6. 231 39. 762 1. 00 26. 86 **ATOM** 1094 CZ PHE 150 6. 437 7. 177 40. 045 1. 00 27. 37

- 182 -ATOM 1095 C PHE 150 2.561 5. 093 44. 808 1. 00 35. 78 ATOM 1096 0 PHE 150 3.095 4. 695 45. 845 1. 00 36. 93 ATOM 1097 N SER 151 1.305 4.813 44. 467 1. 00 38. 60 ATOM 1098 CA SER 151 0.420 4.006 45. 295 1. 00 40. 51 1099 5 ATOM CB SER 151 -0.8304. 802 45.641 1.00 41.51 ATOM 1100 OG SER 151 -1.5075. 159 44. 453 1. 00 47. 40 ATOM 1101 C SER 151 0.038 2. 736 44. 533 1. 00 41. 75 ATOM 1102 0 SER 151 0.069 2.696 43. 301 1. 00 40. 78 ATOM 1103 N PHE 152 -0.3361.704 45. 278 1.00 43.86 10 ATOM 1104 CA PHE 152 -0.6840. 421 44. 687 1. 00 45. 76 **ATOM** 1105 CB PHE 152 0.465 -0.55744. 965 1. 00 51. 67 ATOM 1106 CG PHE 152 0.429 -1.80844. 133 1. 00 57. 82 ATOM 1107 CD1 PHE 152 0.597 -1.74942.751 1. 00 59. 39 ATOM 1108 CD2 PHE 152 0. 256 -3.05644. 739 1. 00 60. 37 15 **ATOM** 1109 CE1 PHE 152 0. 598 -2.91541. 979 1. 00 61. 23 ATOM 1110 CE2 PHE 152 0. 254 -4. 232 43. 978 1.00 61.76 ATOM 1111 CZ PHE 152 0.426 -4.16142. 593 1.00 61.46 ATOM 1112 C PHE 152 -2.007-0. 134 45. 238 1.00 43.74 **ATOM** 1113 0 PHE 152 -2.137-0.38246. 437 1. 00 43. 01 20 ATOM 1114 N PRO 153 -3.005-0.32244. 359 1. 00 40. 65 ATOM 1115 CD PRO 153 -2.9930. 179 42. 979 1. 00 39. 35 ATOM 1116 CA PRO 153 -4. 330 -0. 844 44. 685 1. 00 38. 88 **ATOM** 1117 CB PRO 153 -5. 045 -0.80343. 352 1. 00 36. 16 ATOM 1118 CG PRO 153 -4. 454 0. 359 42.711 1. 00 37. 38 ATOM 25 1119 C PRO 153 -4.235-2.25545. 192 1. 00 41. 30 ATOM 1120 0 PRO 153 -3. 481 -3.05744.657 1. 00 42. 17 ATOM 1121 N VAL 154 -5. 013 -2.56546. 215 1.00 45.30 ATOM 1122 CA VAL 154 -5.016-3.90546. 767 1. 00 49. 50 ATOM 1123 CB VAL 154 -4. 124 -3.98947. 990 1. 00 45. 75

- 183 -ATOM 1124 CG1 VAL 154 **-4**. 297 **-5**. 331 **48**. 638 1. 00 45. 79 ATOM CG2 VAL 154 1125 -2.684 -3.77247. 594 1.00 44.88 ATOM 1126 C VAL 154 -6.432 -4.26847. 181 1. 00 55. 51 **ATOM** 1127 0 VAL 154 -6.963 -3.68348. 119 1.00 58.30 ATOM 1128 N ARG 155 1.00 61.06 5 -7.042-5.23246. 495 ATOM 1129 CA ARG 155 -8. 413 -5. 643 46. 812 1.00 67.71 ATOM 1130 CB ARG 155 -8.812 -6.84745. 956 1.00 71.43 ATOM 1131 CG ARG 155 -9.033-6.50144. 501 1.00 76.11 CD ATOM 1132 ARG 155 **-9.** 094 **−7.** 736 43. 621 1. 00 78. 73 ATOM 1133 NE ARG 155 -7.35210 -9.29242. 226 1.00 81.59 ATOM 1134 CZ ARG 155 -9. 138 -8. 168 41. 190 1. 00 82. 83 ATOM 1135 NH1 ARG 155 -8.778-9. 432 41. 386 1. 00 83. 55 1136 NH2 ARG 155 ATOM -9.340 -7.71739. 956 1. 00 82. 01 ATOM 1137 C -8.639ARG 155 -5. 965 48. 291 1. 00 70. 15 ATOM 1138 0 ARG 155 -7.689-6.25515 49. 022 1. 00 71. 24 ATOM 1139 N HIS 156 -9.903-5.92348. 720 1. 00 71. 23 **ATOM** 1140 CA HIS 156 -10.265-6. 184 50. 117 1. 00 72. 30 1141 CB HIS 156 ATOM -11. 724 -5. 769 50. 365 1. 00 73. 82 ATOM 1142 CG HIS 156 -12.049-5.50651.808 1. 00 76. 32 ATOM 1143 CD2 HIS 156 -11.335-5.72220 52. 941 1. 00 76. 70 **ATOM** 1144 ND1 HIS 156 -13. 243 -4.94452. 211 1.00 76.54 **ATOM** 1145 CE1 HIS 156 -13.251-4.82353. 527 1.00 76.16 ATOM 1146 NE2 HIS 156 -12.106-5.28853.994 1. 00 77. 55 ATOM 1147 C HIS 156 -10.063-7. 645 50. 522 1. 00 72. 42 ATOM 1148 0 HIS 156 25 -9.196-7. 957 51. 345 1. 00 71. 15 ATOM 1149 N ASN 180 11.816 6. 551 32. 482 1. 00 43. 22 CA ASN 180 ATOM 1150 11. 492 7. 278 33. 706 1. 00 42. 73 ATOM 1151 CB ASN 180 12. 677 8. 168 34. 155 1. 00 46. 67 ATOM 1152 CG ASN 180 13. 189 9. 094 33. 052 1. 00 50. 13

- 184 -**ATOM** 1153 OD1 ASN 180 14. 152 8. 777 32. 336 1. 00 51. 24 1154 ND2 ASN 180 ATOM 12. 547 10. 250 32. 915 1. 00 51. 73 ATOM 1155 C ASN 180 10. 228 8. 110 33. 523 1. 00 38. 44 9.941 8.600 ATOM 1156 0 ASN 180 32. 431 1. 00 36. 40 **ATOM** VAL 181 9.473 8. 257 1. 00 34. 02 5 1157 N 34. 603 8.995 ATOM 1158 CA VAL 181 8. 218 34. 577 1. 00 31. 37 8.874 ATOM 1159 CBVAL 181 7. 498 35. 957 1. 00 34. 84 ATOM 1160 CG1 VAL 181 6. 091 9. 484 35. 909 1. 00 32. 59 **ATOM** 1161 CG2 VAL 181 7. 414 7. 405 36. 353 1. 00 38. 00 ATOM 1162 C VAL 181 8. 426 10. 458 34. 221 1. 00 26. 36 10 ATOM 1163 0 VAL 181 7.882 10.964 33. 237 1. 00 23. 28 ATOM 1164 VAL 182 9. 228 N 11. 131 35. 030 1. 00 23. 56 ATOM 1165 CA VAL 182 9. 518 12. 538 34. 826 1. 00 18. 23 ATOM 1166 CB VAL 182 10.702 12. 958 35. 716 1. 00 14. 26 15 ATOM 1167 CG1 VAL 182 11. 905 12. 084 35. 426 1. 00 14. 73 11. 001 ATOM 1168 CG2 VAL 182 14. 403 35. 508 1. 00 11. 08 ATOM 1169 C VAL 182 9.773 12. 882 33. 352 1. 00 15. 36 ATOM 1170 0 9. 330 13. 924 32.875 VAL 182 1. 00 15. 32 **ATOM** 1171 N GLY 183 10.467 12.009 32. 632 1. 00 13. 34 20 ATOM 1172CA GLY 183 10. 713 12. 267 31. 228 1. 00 12. 56 ATOM 1173 C GLY 183 9. 458 12. 098 30. 382 1. 00 13. 06 ATOM 1174 0 GLY 183 9. 104 12. 978 29. 601 1. 00 12. 05 ATOM 1175 N LEU 184 8.772 10.971 30. 540 1. 00 15. 78 7. 549 ATOM 1176 CA LEU 184 10. 708 29. 777 1. 00 15. 21 ATOM 1177 CB LEU 184 6.858 9. 435 25 30. 295 1. 00 16. 78 ATOM 1178 CG LEU 184 7. 613 8. 108 30.075 1. 00 15. 45 1179 CD1 LEU 184 7. 037 7.023 ATOM 30. 951 1. 00 10. 71 ATOM 1180 CD2 LEU 184 7. 548 7. 708 28.608 1. 00 16. 62 ATOM 1181 C LEU 184 6. 601 11. 894 29. 863 1. 00 13. 07

- 185 -ATOM 1182 0 LEU 184 6. 041 12. 311 28. 855 1. 00 13. 90 ATOM 1183 N LEU 185 6. 430 12. 436 31.064 1. 00 11. 99 ATOM CA 1184 LEU 185 5. 571 13.600 31. 250 1. 00 12. 43 ATOM 1185 CBLEU 185 5. 524 13. 997 32. 729 1. 00 13. 27 CG LEU 185 5 ATOM 1186 4. 630 15. 191 33. 080 1. 00 11. 52 ATOM 1187 CD1 LEU 185 3. 256 14. 936 32. 515 1. 00 10. 60 ATOM 1188 CD2 LEU 185 4. 553 15. 395 34. 600 1. 00 12. 16 ATOM 1189 C LEU 185 6.077 14. 788 30. 419 1. 00 12. 48 ATOM 1190 0 LEU 185 5. 289 15. 488 29. 784 1. 00 9. 22 ATOM 1191 N 10 ARG 186 7. 388 15. 020 30. 428 1. 00 13. 24 ATOM 1192 CA ARG 186 7. 946 16. 123 29. 661 1. 00 14. 83 ATOM 1193 CB ARG 186 9. 478 16. 135 29. 727 1. 00 14. 69 ATOM 1194 CGARG 186 10. 112 17. 274 30. 526 1. 00 18. 47 ATOM 1195 CD ARG 186 11. 633 17.063 30.663 1. 00 25. 71 ATOM 1196 15 NE ARG 186 12. 325 18.069 31. 484 1. 00 37. 62 ATOM 1197 CZARG 186 12. 048 18. 357 32. 764 1. 00 42. 54 ATOM 1198 NH1 ARG 186 11.070 17. 721 33. 407 1. 00 43. 86 ATOM 1199 NH2 ARG 186 12. 762 19. 277 33. 414 1. 00 39. 97 -**ATOM** 1200 C ARG 186 7.510 15. 968 28. 220 1. 00 16. 38 **ATOM** 1201 0 20 ARG 186 6.857 16. 851 27. 673 1. 00 17. 00 ATOM 1202 N ASP 187 7.850 14. 832 27. 616 1. 00 19. 34 ATOM 1203 ASP 187 CA 7. 519 14. 579 26. 214 1. 00 24. 04 ATOM 1204 CB ASP 187 7.799 13. 123 25. 822 1. 00 30. 35 ATOM 1205 CG ASP 187 9. 226 12.696 26. 123 1. 00 37. 33 ATOM 25 1206 OD1 ASP 187 9.479 12. 216 27. 251 1. 00 40. 99 ATOM 1207 OD2 ASP 187 10.096 12. 845 25. 234 1. 00 40. 65 **ATOM** 1208 C ASP 187 6.069 14. 889 25. 912 1. 00 23. 78 ATOM 1209 0 ASP 187 5. 756 15. 541 24. 909 1. 00 25. 37 ATOM 1210 N ALA 188 5. 185 14. 413 26. 780 1. 00 20. 98

- 186 -**ATOM** 1211 CA ALA 188 3. 761 14. 634 26. 603 1. 00 17. 11 ATOM 1212 CB ALA 188 2.996 13. 943 27. 722 1. 00 19. 70 ATOM 1213 C ALA 188 3.475 16. 130 26. 600 1. 00 14. 48 ATOM 1214 0 ALA 188 2. 911 16.660 25. 646 1.00 11.69 5 ATOM 1215 N ILE 189 3.873 16. 801 27. 677 1. 00 13. 32 ATOM 1216 CA ILE 189 3. 682 18. 239 27. 817 1. 00 13. 84 ATOM 1217 CB ILE 189 4. 422 18. 754 29.056 1. 00 12. 34 ATOM 1218 CG2 ILE 189 4.368 20. 266 29. 118 1. 00 13. 98 **ATOM** 1219 CG1 ILE 189 3. 776 18. 153 30. 302 1. 00 14. 10 ATOM 1220 10 CD1 ILE 189 4. 455 18. 530 31. 595 1.00 14.04 ATOM 1221 C ILE 189 4. 223 18. 928 26. 575 1. 00 15. 60 ATOM 1222 0 ILE 189 3.634 19. 888 26.058 1. 00 14. 87 ATOM 1223 N LYS 190 5. 351 18. 408 26. 103 1. 00 16. 13 ATOM 1224 CA LYS 190 6. 010 18. 913 24. 918 1.00 16.34 ATOM 15 1225 CB LYS 190 7. 361 18. 211 24. 737 1. 00 18. 43 ATOM 1226 CG LYS 190 8.503 19.081 24. 175 1. 00 24. 32 ATOM 1227 CDLYS 190 8.539 19. 154 22. 631 1. 00 28. 76 ATOM 1228 CE LYS 190 9. 830 19. 841 22. 125 1. 00 30. 07 **ATOM** 1229 NZ LYS 190 10.060 19. 788 20.642 1. 00 27. 01 20 ATOM 1230 C LYS 190 5. 101 18. 652 23. 718 1. 00 16. 41 ATOM 1231 0 LYS 190 4.786 19.575 22. 981 1. 00 17. 80 ATOM 1232 N ARG 191 4.656 17. 413 23. 529 1. 00 14. 92 ATOM 1233 CA ARG 191 3. 798 17. 107 22. 386 1. 00 15. 62 ATOM 1234 CB ARG 191 3. 241 15. 684 22. 491 1. 00 19. 10 ATOM 25 1235 CG ARG 191 4. 071 14. 622 21. 775 1. 00 20. 57 **ATOM** 1236 CDARG 191 3. 634 13. 221 22. 156 1. 00 19. 26 **ATOM** 1237 NE ARG 191 3. 950 12. 925 23. 547 1. 00 23. 45 ATOM ARG 191 1238 CZ3. 732 11. 747 24. 119 1. 00 28. 59 ATOM 1239 NH1 ARG 191 3. 194 10. 767 23. 406 1. 00 32. 19

- 187 -ATOM 1240 NH2 ARG 191 4.062 11. 537 25. 391 1. 00 29. 84 ATOM ARG 191 1241 C 2. 652 18. 086 22. 207 1. 00 15. 44 ATOM 1242 0 ARG 191 2. 383 18. 513 21.098 1. 00 15. 17 ATOM 1243 N ARG 192 1.980 18. 441 23. 295 1.00 17.09 ATOM 5 1244 CA ARG 192 0.853 19. 372 23. 253 1. 00 19. 02 **ATOM** ARG 192 1245 CB 0.588 19.885 24. 647 1.00 17.94 ATOM 1246 CG ARG 192 0.579 18. 785 25. 635 1. 00 20. 35 ATOM 1247 CD ARG 192 -0.81218. 328 25. 855 1. 00 22. 03 ATOM 1248 NE ARG 192 -1.56519. 332 26. 586 1. 00 27. 30 ATOM 10 1249 CZ ARG 192 -2.82419. 164 26. 954 1. 00 32. 13 **ATOM** 1250 NH1 ARG 192 -3. 437 18. 028 26.639 1. 00 34. 51 **ATOM** 1251 NH2 ARG 192 -3. 465 20. 115 27. 631 1. 00 33. 64 ATOM 1252 C ARG 192 1.010 20. 572 22. 321 1. 00 22. 21 ATOM 1253 0 ARG 192 0.017 21. 184 21. 937 1. 00 24. 03 **ATOM** 15 1254 N GLY 193 2. 245 20. 923 21. 975 1. 00 24. 28 ATOM 1255 CA GLY 193 2. 472 22. 052 21.088 1. 00 25. 59 **ATOM** 1256 C GLY 193 2. 351 23. 417 21. 750 1. 00 27. 55 ATOM 1257 0 GLY 193 2. 734 24. 437 21. 163 1. 00 26. 53 **ATOM** 1258 N ASP 194 1. 836 22. 981 23. 434 1. 00 28. 09 20 ATOM 1259 ASP 194 CA 1. 634 24. 678 23. 725 1. 00 28. 74 ATOM 1260 CB ASP 194 0. 349 24. 597 24. 548 1. 00 32. 11 ATOM 1261 CG ASP 194 -0. 873 24. 329 23. 692 1. 00 36. 60 ATOM 1262 OD1 ASP 194 -1.05325. 025 22. 668 1. 00 38. 48 ATOM 1263 OD2 ASP 194 -1.65923. 424 24.046 1. 00 40. 23 ATOM 25 1264 C ASP 194 2. 774 25. 089 24. 641 1.00 27.04 ATOM 1265 0 ASP 194 3. 815 24. 439 24. 689 1. 00 26. 55 ATOM 1266 N PHE 195 2. 565 26. 181 25. 370 1. 00 25. 47 ATOM 1267 PHE 195 CA 3. 582 26. 691 26. 274 1. 00 25. 41 ATOM 1268 CBPHE 195 3. 083 27. 932 27. 016 1. 00 27. 05

- 188 -**ATOM** 1269 CG PHE 195 1. 00 28. 43 3. 156 29. 192 26. 201 ATOM CD1 PHE 195 1.00 31.56 1270 2. 032 29. 686 25. 550 CD2 PHE 195 ATOM 1271 4. 353 29. 880 26.067 1. 00 29. 11 ATOM 1272 CE1 PHE 195 2.097 30. 852 24. 771 1. 00 30. 45 CE2 PHE 195 ATOM 1273 4. 426 31. 046 25. 290 5 1. 00 30. 62 ATOM 1274 CZPHE 195 3. 294 31. 528 24.644 1. 00 29. 47 ATOM 1275 C PHE 195 4. 024 25. 642 27. 267 1. 00 24. 15 ATOM 1276 0 PHE 195 3. 214 25. 083 28. 000 1. 00 25. 61 1277 ATOM N GLU 196 5. 324 25. 385 27. 280 1. 00 22. 49 ATOM 1278 CA GLU 196 5. 897 24. 394 10 28. 166 1. 00 23. 12 ATOM 1279 CB GLU 196 7. 117 23. 754 27. 499 1. 00 21. 72 1280 ATOM CG GLU 196 6. 942 23. 418 1. 00 22. 22 26. 020 ATOM 1281 CD GLU 196 8. 121 22. 629 25. 477 1. 00 24. 60 0E1 GLU 196 1282 8.336 ATOM 22. 601 24. 241 1. 00 23. 54 1283 0E2 GLU 196 15 ATOM 8.839 22. 026 26.301 1. 00 26. 49 1284 C ATOM GLU 196 6. 314 25. 066 29. 466 1. 00 24. 25 1285 24. 966 ATOM 0 GLU 196 7.467 29.882 1. 00 26. 05 ATOM 1286 N 5. 376 25.729 MET 197 30. 126 1. 00 25. 12 ATOM 1287 5. 711 CA MET 197 26. 444 31. 352 1. 00 27. 52 1288 20 ATOM CBMET 197 5. 546 27. 942 31.096 1. 00 29. 51 ATOM 1289 CG MET 197 6. 758 28. 782 31.466 1. 00 33. 61 1290 SD MET 197 7. 208 29. 992 ATOM 30. 181 1. 00 35. 72 1291 5.967 ATOM CE MET 197 31. 256 30.466 1. 00 37. 45 4.906 ATOM 1292 C MET 197 26. 045 32. 583 1. 00 27. 47 25 ATOM 1293 0 MET 197 4. 921 26. 749 33. 597 1. 00 25. 63 ATOM 1294 N ASP 198 4. 230 24. 903 32. 502 1. 00 27. 57 ATOM 1295 CA ASP 198 3. 384 24. 430 33. 598 1. 00 26. 12 ATOM ASP 198 1296 CB 2. 462 23. 298 33. 110 1. 00 29. 89 ATOM 1297 CG ASP 198 1. 326 23. 796 32. 232 1. 00 31. 76

- 189 -ATOM 1298 OD1 ASP 198 0. 736 24. 840 32. 590 1. 00 30. 59 ATOM 1299 OD2 ASP 198 1. 023 23. 135 31. 203 1. 00 32. 71 ATOM 1300 C ASP 198 4. 110 23. 959 34. 853 1. 00 22. 26 ATOM 1301 0 ASP 198 3.960 24. 551 35. 923 1.00 18.00 5 ATOM 1302 N VAL 199 4.873 22. 878 34. 717 1.00 19.81 **ATOM** 1303 CA VAL 199 5.605 22. 301 35. 841 1. 00 18. 78 **ATOM** 1304 CBVAL 199 5. 133 20.852 36. 115 1. 00 16. 48 **ATOM** 1305 CG1 VAL 199 3.736 20. 859 36. 696 1. 00 19. 07 ATOM 1306 CG2 VAL 199 5. 150 20.042 34. 823 1. 00 10. 86 10 ATOM 1307 C VAL 199 7. 121 22. 267 35. 648 1. 00 20. 19 ATOM 1308 0 VAL 199 7.665 22. 752 34. 655 1. 00 21. 16 ATOM 1309 N VAL 200 7.798 21. 695 36. 629 1. 00 20. 40 ATOM 1310 CA VAL 200 9. 237 21. 547 36. 594 1. 00 22. 39 ATOM 1311 CB VAL 200 9. 975 22. 834 37. 007 1. 00 24. 84 ATOM 1312 CG1 VAL 200 15 9. 331 23. 406 38. 255 1. 00 31. 58 ATOM 1313 CG2 VAL 200 11.465 22. 539 37. 266 1.00 21.54 ATOM 1314 C VAL 200 9.502 20. 457 37. 598 1.00 23.06 ATOM 1315 0 VAL 200 9.039 20. 501 38. 755 1. 00 22. 26 ATOM 1316 N ALA 201 10. 229 19. 460 37. 120 1. 00 23. 03 20 ATOM 1317 CA ALA 201 10.569 18. 300 37. 907 1. 00 22. 74 ATOM 1318 CB ALA 201 11.460 17. 418 37. 112 1. 00 23. 66 ATOM 1319 С ALA 201 11. 236 18. 646 39. 209 1. 00 24. 47 ATOM 1320 0 ALA 201 12.045 19. 564 39. 285 1. 00 27. 55 ATOM 1321 N MET 202 10.872 17. 914 40. 244 1. 00 25. 96 25 ATOM 1322 CA MET 202 11.479 18. 106 41. 547 1. 00 27. 52 ATOM 1323 CB MET 202 10.720 19. 124 42. 386 1. 00 27. 45 ATOM 1324 CG MET 202 43. 597 11. 516 19. 580 1. 00 27. 56 ATOM 1325 SD MET 202 11. 967 18. 244 44. 740 1. 00 28. 85 ATOM 1326 CE MET 202 10. 732 18. 486 46. 045 1. 00 23. 74

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- 190 -**ATOM** 1327 C MET 202 11. 436 16. 752 42. 219 1.00 28.79 ATOM 1328 0 MET 202 10. 377 16. 290 42. 653 1. 00 25. 51 **ATOM** 1329 VAL 203 N 12.600 16. 118 42. 293 1. 00 29. 76 ATOM 1330 CA VAL 203 12. 695 14. 802 42. 883 1. 00 28. 97 5 ATOM 1331 CB VAL 203 12. 943 13. 727 41. 813 1. 00 25. 86 ATOM 1332 CG1 VAL 203 11. 936 13.870 40.681 1. 00 22. 02 ATOM 1333 CG2 VAL 203 14. 361 13.831 41. 310 1. 00 23. 30 **ATOM** 1334 C VAL 203 13.815 14. 713 43. 890 1. 00 31. 36 ATOM 1335 0 VAL 203 13. 934 13. 713 44. 585 1. 00 34. 93 ATOM 10 1336 N ASN 204 14. 638 15. 745 43. 987 1. 00 32. 12 ATOM 1337 CA ASN 204 15. 741 15. 674 44. 929 1. 00 33. 37 ATOM 1338 CB ASN 204 16.667 16.867 44. 736 1. 00 36. 19 ATOM 1339 CG ASN 204 18.052 16.601 45. 260 1. 00 39. 20 ATOM 1340 OD1 ASN 204 18.847 15. 905 44. 621 1. 00 41. 71 ATOM 15 1341 ND2 ASN 204 18. 349 17. 133 46. 440 1. 00 39. 72 ATOM 1342 C ASN 204 15. 220 15. 625 46. 363 1. 00 32. 02 ATOM 1343 0 ASN 204 14. 382 16. 439 46. 751 1. 00 28. 87 ATOM 1344 ASP 205 N 15: 705 14. 665 47. 149 1. 00 31. 97 ATOM 1345 CA ASP 205 15. 245 14. 538 48. 541 1. 00 33. 94 20 ATOM 1346 CB ASP 205 15. 792 13. 266 49. 197 1. 00 32. 38 ATOM 1347 CG ASP 205 15. 163 12. 017 48. 642 1. 00 31. 18 ATOM 1348 OD1 ASP 205 15. 386 10. 935 49. 217 1. 00 31. 15 **ATOM** OD2 ASP 205 1349 12. 118 14. 450 47. 625 1. 00 28. 42 ATOM 1350 C ASP 205 15. 626 15. 722 49. 414 1. 00 33. 64 25 ATOM 1351 0 ASP 205 14.909 16. 080 50. 356 1. 00 33. 83 ATOM 1352 N THR 206 16. 770 16. 313 49. 092 1. 00 31. 15 ATOM 1353 CA THR 206 17. 290 17. 449 49. 826 1. 00 25. 09 ATOM 1354 CBTHR 206 18. 646 17. 825 49. 278 1. 00 25. 45 ATOM OG1 THR 206

19. 423

16. 630

49. 123

1. 00 24. 81

1355

- 191 -ATOM 1356 CG2 THR 206 19. 350 18. 769 50. 232 1. 00 26. 26 ATOM 1. 00 20. 16 1357 C THR 206 16. 347 18. 634 49. 734 **ATOM** 1358 THR 206 15. 923 0 19. 184 50. 755 1.00 17.86 ATOM 1359 N VAL 207 16.009 19.016 48. 510 1. 00 12. 86 1360 VAL 207 ATOM CA 15. 106 20. 133 48. 308 1.00 9.27 5 **ATOM** 1361 CB VAL 207 14. 582 20. 164 46. 867 1.00 5. 21 ATOM 1362 CG1 VAL 207 13. 555 21. 243 46. 720 1. 00 1. 26 **ATOM** 1363 CG2 VAL 207 15. 714 20. 397 45. 910 1.00 4.57 ATOM 1364 C VAL 207 13. 917 19. 992 49. 255 1. 00 11. 72 10 ATOM 1365 0 VAL 207 13. 584 20. 909 50.016 1.00 9.00 1366 ATOM N ALA 208 13. 291 18. 819 49. 212 1.00 14.04 ATOM 1367 ALA 208 12. 122 18. 523 CA 50. 041 1. 00 14. 67 1368 ALA 208 11.598 ATOM CB17. 148 49. 702 1.00 14.60 ATOM 1369 C ALA 208 12. 422 18. 615 51. 537 1. 00 15. 41 1370 15 ATOM 0 ALA 208 11. 514 18. 770 52. 362 1. 00 14. 28 ATOM 1371 N THR 209 13.699 18. 498 51.879 1. 00 13. 94 ATOM 1372 CA THR 209 14. 123 18. 591 53. 261 1. 00 13. 05 ATOM 1373 CB THR 209 15.567 18. 237 53. 423 1.00 11.66 ATOM 1374 OG1 THR 209 15.887 17. 177 52. 525 1. 00 12. 70 20 ATOM 1375 CG2 THR 209 15.833 17.807 54. 846 1. 00 7. 92 1376 THR 209 14.007 ATOM C 20.041 53.626 1. 00 14. 97 ATOM 1377 0 THR 209 13. 554 20. 401 54. 714 1. 00 14. 80 ATOM 1378 MET 210 N. 14. 447 20. 885 52. 707 1.00 15.34 ATOM 1379 CA MET 210 14. 363 22. 298 52. 965 1. 00 16. 36 25 ATOM 1380 CB MET 210 15.043 23.091 51.845 1. 00 19. 89 **ATOM** 1381 CG MET 210 15. 119 24. 592 52. 103 1. 00 23. 82 ATOM 1382 SD MET 210 15. 258 25. 542 50. 561 1. 00 29. 33 ATOM 1383 CE MET 210 13. 547 25. 995 50. 325 1. 00 27. 80 ATOM 1384 C MET 210 12.864 22. 592 53. 031 1. 00 14. 33

- 192 -**ATOM** 1385 MET 210 0 12. 332 22. 896 54. 102 1. 00 15. 04 1386 ATOM N ILE 211 12. 180 22. 452 51.898 1. 00 11. 15 ATOM 1387 CA ILE 211 10. 743 22. 708 51. 831 1.00 9.09 ATOM 1388 CB ILE 211 10.157 22. 122 50. 566 1. 00 5. 39 ATOM 1389 CG2 ILE 211 5 8. 748 22. 693 50. 337 1. 00 3. 22 ATOM 1390 CG1 ILE 211 11. 111 22. 412 49. 412 1. 00 2. 02 ATOM 1391 CD1 ILE 211 10.580 22.065 48. 067 1.00 1.00 ATOM 1392 C ILE 211 9. 987 22. 129 53. 022 1. 00 10. 92 ATOM 1393 0 ILE 211 9. 117 22. 781 53.605 1. 00 7. 92 1394 10 ATOM N SER 212 10. 319 20. 891 53. 364 1. 00 12. 74 ATOM 1395 SER 212 CA 9.701 20. 254 54. 489 1. 00 15. 18 **ATOM** 1396 CB SER 212 10.300 18. 880 54. 704 1. 00 12. 84 ATOM 1397 0G SER 212 10.216 18. 533 56. 078 1. 00 19. 56 ATOM 1398 C SER 212 9. 918 21. 101 55. 736 1. 00 19. 90 ATOM 1399 15 0 SER 212 8. 969 21. 432 56. 435 1. 00 21. 30 ATOM 1400 N CYS 213 11. 161 21. 476 56. 016 1. 00 24. 22 ATOM 1401 CA CYS 213 11. 432 22. 259 57. 219 1. 00 28. 52 ATOM 1402 CB CYS 213 12. 934 22. 367 57. 464 1. 00 30. 65 **ATOM** 1403 SG CYS 213 13.713 20. 766 57. 805 1. 00 39. 09 **ATOM** 20 1404 C CYS 213 10.822 23. 637 57. 168 1. 00 29. 40 ATOM 1405 0 CYS 213 10.366 24. 150 58. 186 1.00 30.64 ATOM 1406 TYR 214 N 10.816 24. 229 55.981 1. 00 29. 50 ATOM 1407 TYR 214 CA 10. 243 25. 548 55. 788 1. 00 29. 27 ATOM 1408 CB TYR 214 10. 168 25. 846 54. 292 1. 00 31. 33 25 ATOM 1409 CG TYR 214 9.637 27. 212 53. 985 1. 00 33. 15 ATOM 1410 CD1 TYR 214 10. 182 28. 328 54. 594 1. 00 36. 28 ATOM 1411 CE1 TYR 214 9.694 29. 592 54. 341 1. 00 39. 73 **ATOM** 1412 CD2 TYR 214 8. 582 27. 390 53. 100 1. 00 35. 23 ATOM 1413 CE2 TYR 214 8. 080 28. 656 52. 833 1. 00 39. 38

- 193 -**ATOM** TYR 214 1. 00 41. 11 1414 CZ8. 644 29. 758 53. 463 ATOM TYR 214 1. 00 43. 33 1415 0H8. 168 31. 034 53. 241 TYR 214 25. 649 56. 429 **ATOM** 1416 C 8.848 1. 00 28. 57 TYR 214 8.561 26. 578 57. 185 1. 00 27. 99 ATOM 1417 0 ATOM 1418 N TYR 215 7. 986 24. 685 56. 136 1. 00 27. 91 5 24.685 ATOM 1419 CA TYR 215 6.642 56. 691 1. 00 27. 12 1420 CBTYR 215 5.922 23. 403 1. 00 21. 95 ATOM 56. 309 5. 723 **ATOM** 1421 CG TYR 215 23. 235 54. 829 1. 00 18. 06 ATOM 1422 CD1 TYR 215 6.064 22. 048 54. 197 1. 00 17. 25 1423 CE1 TYR 215 5. 835 10 ATOM 21. 867 52. 841 1. 00 17. 47 ATOM 1424 CD2 TYR 215 5. 152 24. 246 54.065 1. 00 16. 51 CE2 TYR 215 4.917 24. 075 52. 711 1. 00 15. 51 ATOM 1425 1426 5. 257 22. 882 52. 109 ATOM CZ TYR 215 1. 00 17. 82 ATOM 1427 0HTYR 215 4. 979 22. 681 50. 785 1. 00 20. 98 1428 6.658 24. 810 ATOM C TYR 215 58. 201 1. 00 30. 19 15 5. 780 ATOM 14290 TYR 215 25. 438 58. 778 1. 00 31. 10 1430 GLU 216 7.640 24. 197 **ATOM** N 58. 850 1. 00 35. 15 7.725 24. 278 60. 306 ATOM 1431 CA GLU 216 1. 00 41. 19 8.560 ATOM 1432 CB GLU 216 23. 132 60. 876 1. 00 44. 10 1433 CG GLU 216 7.877 21. 767 60.887 20 ATOM 1. 00 52. 19 6.579 21.749 ATOM 1434 CD GLU 216 61. 685 1. 00 54. 93 ATOM 1435 OE1 GLU 216 6. 491 22. 481 62. 702 1. 00 55. 44 1436 0E2 GLU 216 5.658 20. 988 61. 296 1. 00 56. 26 ATOM 8.369 25. 591 ATOM 1437 C GLU 216 60. 707 1. 00 43. 33 1438 **GLU 216** 7. 787 26. 385 1.00 44.64 25 ATOM 0 61. 449 ATOM 1439 N ASP 217 9. 583 25. 802 60. 209 1. 00 44. 35 10. 357 27. 007 ATOM 1440 CA ASP 217 60. 489 1. 00 44. 65 ATOM 1441 CBASP 217 11. 734 26. 623 61. 033 1. 00 47. 71 1442 CG ASP 217 12.667 27. 806 ATOM 61. 136 1. 00 50. 46

- 194 -ATOM 1443 OD1 ASP 217 13. 252 28. 205 60. 106 1. 00 51. 95 ATOM OD2 ASP 217 1444 12. 804 28. 346 62. 252 1. 00 54. 06 **ATOM** 1445 C ASP 217 10. 514 27. 820 59. 215 1. 00 43. 04 ATOM 1446 0 ASP 217 11. 372 27. 527 58. 385 1. 00 44. 60 **ATOM** 1447 HIS 218 9.691 5 N 28. 848 59.059 1. 00 41. 00 ATOM 1448 HIS 218 9.750 29.671 CA 57. 862 1. 00 39. 42 ATOM 1449 CBHIS 218 8.569 30.630 57. 826 1. 00 40. 46 CG HIS 218 **ATOM** 1450 7. 261 29. 960 58. 083 1. 00 44. 54 ATOM 1451 CD2 HIS 218 6.652 28. 930 57. 450 1. 00 45. 30 ATOM 1452 10 ND1 HIS 218 6. 449 30. 290 59. 147 1. 00 47. 09 1453 ATOM: CE1 HIS 218 5. 397 29. 492 59. 161 1. 00 45. 61 NE2 HIS 218 ATOM 1454 28.657 5. 497 58. 142 1. 00 46. 44 ATOM 1455 C HIS 218 11.036 30. 452 57. 759 1. 00 37. 69 1456 ATOM HIS 218 1. 00 37. 21 0 11. 120 31. 381 56. 974 15 **ATOM** 1457 N GLN 219 12. 041 30.076 58. 537 1. 00 37. 38 ATOM 1458 13. 312 CA GLN 219 30. 779 58. 494 1. 00 38. 18 ATOM 1459 CB GLN 219 13. 727 31. 186 59. 910 1. 00 41. 72 **ATOM** 1460 CG 14. 577 GLN 219 32. 451 60.011 1. 00 48. 69 **ATOM** 1461 CD GLN 219 13.836 33. 718 59. 546 1. 00 55. 14 12. 665 ATOM 1462 20 OE1 GLN 219 33. 945 59. 908 1. 00 55. 89 ATOM 1463 NE2 GLN 219 14. 523 34. 555 58. 751 1. 00 55. 41 1464 ATOM C GLN 219 14. 348 29. 846 57. 886 1. 00 36. 85 **ATOM** 1465 0 GLN 219 15.508 30. 200 57. 735 1. 00 37. 28 ATOM 1466 N CYS 220 13. 912 28. 647 57. 535 1. 00 36. 02 ATOM 1467 CYS 220 14.790 25 CA 27. 646 56. 950 1. 00 37. 10 ATOM 1468 CB CYS 220 14. 103 26. 286 57. 043 1. 00 38. 40 ATOM 1469 CYS 220 15.067 SG 24. 916 56. 396 1. 00 44. 24 ATOM 1470 C CYS 220 15. 106 27. 970 55. 486 1. 00 37. 48 ATOM 1471 0 CYS 220 14. 193 28. 081 54. 672 1. 00 40. 52

- 195 -ATOM 1472 N GLU 221 16. 382 28. 123 55. 137 1.00 36.17 **ATOM** 1473 GLU 221 16. 742 28. 428 53. 746 1. 00 35. 58 CA ATOM 1474 CB GLU 221 17. 116 29. 911 53. 591 1.00 38.60 15. 921 30.878 ATOM 1475 CG GLU 221 53. 645 1. 00 42. 48 1476 GLU 221 16.325 32. 347 5 ATOM CD 53. 760 1. 00 42. 62 ATOM 1477 OE1 GLU 221 17. 120 32. 815 52.909 1. 00 42. 89 ATOM 1478 0E2 GLU 221 15. 835 33. 024 54. 700 1.00 40.36 1479 C GLU 221 17. 896 ATOM 27. 566 53. 260 1. 00 33. 89 1480 0 ATOM GLU 221 18. 498 27. 826 52. 217 1. 00 32. 29 ATOM 1481 VAL 222 18. 199 26. 525 1.00 32.57 N 54.018 10 ATOM 1482 CA VAL 222 19. 286 25. 654 53.645 1.00 31.01 ATOM 1483 CB VAL 222 20. 548 26. 041 54. 376 1. 00 29. 59 ATOM 1484 CG1 VAL 222 21.673 25. 102 1.00 29.07 53. 995 **ATOM** 1485 CG2 VAL 222 20.895 27. 465 54. 043 1. 00 30. 00 ATOM 1486 C VAL 222 18.983 24. 214 53. 966 1. 00 31. 75 15 ATOM 1487 0 VAL 222 18.872 23. 846 55. 132 1. 00 33. 50 ATOM 1488 N **GLY 223** 18.858 23. 400 52. 925 1. 00 31. 02 ATOM 1489 CA GLY 223 18. 575 21. 994 53. 119 1. 00 28. 49 ATOM 1490 C GLY 223 19. 847 21. 184 53. 026 1. 00 26. 21 ATOM 1491 0 **GLY 223** 20. 757 21. 528 52. 267 20 1. 00 25. 39 ATOM 1492 N MET 224 19. 911 20.098 53. 786 1. 00 24. 93 **ATOM** 1493 **MET 224** 21. 101 19. 267 CA 53. 774 1. 00 24. 66 ATOM 1494 CB MET 224 22. 164 19. 958 54. 623 1. 00 26. 07 23. 584 1. 00 26. 25 ATOM 1495 CG MET 224 19. 535 54. 358 **ATOM** 1496 MET 224 24.664 20. 375 25 SD 55. 525 1. 00 28. 76 **ATOM** 1497 CE MET 224 24. 493 19. 328 56. 939 1. 00 27. 46 **ATOM** 1498 MET 224 20.867 17. 819 C 54. 253 1. 00 23. 62 MET 224 20. 243 ATOM 1499 17. 581 55. 294 1. 00 21. 62 0 ATOM 1500 N ILE 225 21. 389 16. 867 53. 478 1. 00 21. 96

- 196 -**ATOM** 1501 CA ILE 225 21. 265 15. 434 53. 764 1. 00 21. 80 ATOM 1502 CB ILE 225 20. 514 14. 706 52. 662 1. 00 23. 26 ATOM 1503 CG2 ILE 225 20. 389 13. 242 53.026 1. 00 22. 57 ATOM 1504 CG1 ILE 225 19. 142 15. 332 52. 463 1. 00 26. 22 CD1 ILE 225 5 ATOM 1505 18. 270 15. 229 53.688 1. 00 30. 06 ATOM 1506 C ILE 225 22. 595 14. 702 53. 904 1. 00 21. 76 ATOM 1507 0 ILE 225 23. 204 14. 299 52. 909 1. 00 20. 84 **ATOM** 1508 N VAL 226 23. 008 14. 492 55. 146 1. 00 22. 14 ATOM 1509 CA VAL 226 24. 263 13. 824 55. 454 1. 00 22. 07 10 ATOM 1510 CB VAL 226 25. 031 14. 613 56. 514 1. 00 22. 20 ATOM 1511 CG1 VAL 226 26. 321 13. 905 56. 872 1. 00 20. 57 **ATOM** 1512 CG2 VAL 226 25. 283 16. 016 56. 005 1. 00 22. 66 ATOM 1513 C VAL 226 24.060 12. 411 55. 972 1. 00 22. 96 ATOM 1514 0 VAL 226 24. 032 12. 172 57. 183 1. 00 23. 79 15 ATOM 1515 N GLY 227 23. 924 11. 470 55.054 1. 00 23. 08 ATOM 1516 CA GLY 227 23. 738 10. 094 55. 459 1. 00 25. 20 ATOM 1517 C **GLY 227** 24. 623 9. 207 54. 621 1. 00 25. 79 ATOM 1518 0 GLY 227 25.820 9. 447 54. 501 1. 00 26. 18 ATOM 1519 N THR 228 24. 039 8. 181 54. 026 1. 00 27. 28 20 ATOM 1520 CA THR 228 24. 822 7. 291 53. 200 1.00 29.44 ATOM 1521 CBTHR 228 23.900 6. 356 52. 413 1.00 28.91 ATOM 1522 OG1 THR 228 24. 691 5. 441 51.650 1.00 27.54 ATOM 1523 CG2 THR 228 22. 983 7. 159 51. 496 1.00 30.69 **ATOM** 1524 C THR 228 25. 705 8. 139 52. 267 1. 00 30. 87 25 **ATOM** 1525 0 THR 228 26.878 7.834 52. 072 1.00 32.00 ATOM 1526 N GLY 229 25. 140 9. 216 51. 723 1. 00 31. 23 **ATOM** 1527 CA GLY 229 25. 888 10. 111 50. 855 1. 00 30. 25 **ATOM** 1528 C GLY 229 25. 716 11. 501 51. 434 1. 00 32. 12 ATOM 1529 0 GLY 229 25. 139 11. 632 52. 518 1. 00 33. 23

- 197 -CYS 230 ATOM 1530 N 26. 208 12. 535 50. 749 1. 00 31. 95 ATOM 1531 CA CYS 230 26. 057 13. 909 51. 247 1. 00 31. 05 CBCYS 230 27. 344 ATOM 1532 14. 417 51. 891 1. 00 31. 11 1533 CYS 230 27. 145 16.090 52. 562 ATOM SG 1.00 40.64 CYS 230 1534 C 25.650 14. 909 5 ATOM 50. 183 1.00 29.04 1535 CYS 230 26. 202 14.913 ATOM 0 49. 087 1.00 30.85 ATOM 1536 ASN 231 24. 701 15. 775 50. 513 1. 00 26. 12 N 1537 ASN 231 24. 267 16. 773 ATOM CA 49. 554 1. 00 26. 17 ATOM 1538 CBASN 231 23. 380 16. 130 48. 505 1. 00 24. 13 1539 ASN 231 ATOM CG 23. 146 17. 030 47. 341 1.00 24.98 10 **ATOM** 1540 OD1 ASN 231 22. 505 18.064 47. 463 1. 00 24. 73 ND2 ASN 231 ATOM 1541 23. 684 16. 656 46. 196 1.00 29.51 ATOM 1542 C ASN 231 23. 529 17. 927 50. 213 1. 00 27. 77 **ATOM** 1543 ASN 231 22. 929 17. 757 1. 00 28. 70 0 51. 275 15 ATOM 1544 N **ALA 232** 23. 569 19. 103 49. 587 1.00 27.44 22.890 20. 258 ATOM 1545 CA ALA 232 50. 158 1. 00 26. 70 ATOM 1546 CB ALA 232 23. 806 20. 963 51. 113 1. 00 26. 89 ATOM 1547 C ALA 232 22. 366 21. 245 49. 144 1. 00 26. 61 ATOM 1548 0 ALA 232 22. 693 21. 184 47. 963 1. 00 26. 44 ATOM 1549 N CYS 233 21. 537 22. 161 49. 617 20 1. 00 27. 04 ATOM 1550 CA CYS 233 20.976 23. 172 48. 743 1. 00 31. 21 CYS 233 19.676 22.666 **ATOM** 1551 CB 48. 127 1.00 31.60 **ATOM** 1552 SG CYS 233 18. 376 22. 446 49.348 1.00 35.31 **ATOM** 1553 C CYS 233 20. 708 24. 408 49. 589 1. 00 31. 98 ATOM 1554 0 CYS 233 20. 596 24. 303 50.809 1. 00 32. 62 25 1555 TYR 234 20.621 25. 572 ATOM N 48. 949 1. 00 30. 70 ATOM 1556 CA TYR 234 20.366 26. 822 49.660 1.00 30.60 ATOM 1557 CB TYR 234 21. 684 27. 524 50.026 1. 00 29. 53 ATOM 1558 CG TYR 234 22. 464 28. 011 48. 829 1. 00 27. 41

- 198 -1. 00 25. 56 ATOM 1559 CD1 TYR 234 22. 363 29. 327 48. 393 ATOM 1560 CE1 TYR 234 22. 981 29. 739 47. 217 1.00 25.47 ATOM 1561 CD2 TYR 234 23. 218 27. 121 48.061 1. 00 28. 10 CE2 TYR 234 23. 838 27. 524 46. 882 1. 00 26. 39 ATOM 1562 28.830 1. 00 25. 77 5 ATOM 1563 CZTYR 234 23. 707 46. 462 TYR 234 29. 201 45. 253 1. 00 27. 36 ATOM OH 24. 240 1564 **ATOM** 1565 C TYR 234 19.531 27. 742 48. 797 1. 00 32. 10 1. 00 32. 79 **ATOM** 1566 0 TYR 234 19. 211 27. 411 47. 657 MET 235 19. 184 28. 897 49. 357 1. 00 34. 08 ATOM 1567 N ATOM MET 235 18. 380 29. 908 48. 679 1. 00 34. 57 10 1568 CA MET 235 17. 492 30.617 49.697 1.00 34.74 ATOM 1569 CB ATOM 1570 CG MET 235 16. 489 29.699 50. 305 1. 00 34. 74 MET 235 1.00 35.81 ATOM SD 15. 575 28. 985 48. 959 1571 ATOM 1572 CE MET 235 14. 171 30. 092 48. 917 1.00 34.50 ATOM 1573 C MET 235 19. 270 30. 933 48. 009 1.00 35.41 15 MET 235 31. 930 ATOM 1574 0 19. 631 48. 625 1.00 37.55 19.626 30. 702 46. 753 1. 00 35. 58 MOTA 1575 N GLU 236 ATOM 46. 049 1. 00 36. 59 1576 CA GLU 236 20. 487 31. 643 ATOM 1577 CB **GLU 236** 21. 168 30. 949 44. 869 1.00 38.16 20 ATOM 1578 CG GLU 236 22. 051 31.861 44. 051 1. 00 39. 44 ATOM CD GLU 236 23. 107 32. 542 44. 890 1.00 41.44 1579 31. 891 ATOM 1580 OE1 GLU 236 24. 116 45. 240 1.00 40.65 ATOM 1581 OE2 GLU 236 22.918 33. 735 45. 208 1. 00 42. 03 32. 838 ATOM 1582 C GLU 236 19.679 45. 564 1. 00 37. 02 ATOM GLU 236 18. 452 32. 810 45. 580 1.00 38.00 1583 0 25 ATOM 1584 N GLU 237 20. 354 33. 898 45. 149 1. 00 38. 75 GLU 237 19.634 35.062 44.668 1. 00 41. 18 ATOM 1585 CA ATOM 1586 CBGLU 237 20. 482 36. 317 44. 830 1. 00 39. 63 CG 36. 579 46. 258 1. 00 36. 10 ATOM 1587 GLU 237 20. 912

- 199 -37. 022 47. 131 1.00 35.20 CD GLU 237 19. 764 **ATOM** 1588 37. 971 1. 00 34. 49 **ATOM** 1589 0E1 GLU 237 19.056 46. 726 1.00 33.72 36. 434 48. 221 ATOM 1590 0E2 GLU 237 19. 574 19. 307 34. 836 43. 206 1. 00 43. 71 C GLU 237 ATOM 1591 42. 437 1. 00 43. 65 GLU 237 20. 143 34. 351 ATOM 1592 0 42. 832 1. 00 45. 47 MET 238 18. 078 35. 172 ATOM 1593 N 17.625 35.013 41. 457 1. 00 47. 13 **ATOM** 1594 CA MET 238 41. 275 1. 00 47. 10 MET 238 16. 275 35. 705 ATOM 1595 CB 41. 721 1. 00 46. 82 ATOM 1596 MET 238 15. 094 34. 875 CG 40.554 1.00 45.37 MET 238 14.773 33. 548 ATOM 1597 SD 10 39. 412 1. 00 46. 47 **ATOM** CE MET 238 13. 564 34. 332 1598 40. 466 1. 00 48. 34 MET 238 18. 629 35. 589 ATOM 1599 C 1.00 49.97 MET 238 18. 814 35. 061 39. 371 ATOM 1600 0 40.868 1.00 48.44 **GLN 239** 19. 280 36. 672 **ATOM** 1601 N 40.026 1. 00 49. 76 ATOM 1602 CA GLN 239 20. 252 37. 344 15 1.00 54.00 20. 398 38. 794 40. 491 MOTA 1603 CBGLN 239 1.00 58.66 GLN 239 20. 375 38. 963 42. 007 ATOM 1604 CG 1.00 63.23 40. 394 42. 447 CD GLN 239 20.056 MOTA 1605 40. 624 43. 593 1.00 65.75 ATOM 1606 OE1 GLN 239 19.660 41. 540 1. 00 63. 23 20. 233 41. 359 ATOM 1607 NE2 GLN 239 20 36.665 40.011 1. 00 48. 87 **ATOM** C GLN 239 21.612 1608 37. 295 39.687 1. 00 49. 50 22.611 GLN 239 ATOM 1609 0 21.656 35. 384 40. 354 1. 00 47. 67 **ATOM** 1610 N ASN 240 34. 660 40. 379 1. 00 47. 01 ASN 240 22. 926 ATOM 1611 CA 41. 809 1.00 47.66 ATOM ASN 240 23. 301 34. 278 1612 CB 25 1. 00 45. 71 35. 347 42. 518 1613 ASN 240 24. 101 ATOM CG 43. 021 1. 00 43. 88 ATOM OD1 ASN 240 23. 553 36. 328 1614 1.00 46.64 ND2 ASN 240 35. 159 42. 561 ATOM 1615 25. 414

C

1616

ASN 240

ATOM

39. 550

1. 00 46. 58

33. 393

22. 861

5

- 200 -ATOM 1617 · 0 ASN 240 23. 888 32. 840 39. 137 1. 00 46. 44 ATOM 1618 VAL 241 N 21. 643 32. 919 39. 340 1. 00 44. 69 ATOM 1619 VAL 241 21.426 31. 717 CA 38. 564 1. 00 43. 22 ATOM 1620 CB VAL 241 20. 103 31.056 38. 948 1. 00 43. 93 ATOM 1621 CG1 VAL 241 20.071 29. 643 5 38. 412 1. 00 44. 87 ATOM 1622 CG2 VAL 241 19. 922 31.091 40. 456 1. 00 40. 98 1623 ATOM C VAL 241 21. 358 32. 182 37. 126 1. 00 41. 83 1624 ATOM 0 VAL 241 20. 351 32. 739 36. 685 1. 00 42. 56 1625 ATOM **GLU 242** 22. 433 31.974 N 36. 386 1. 00 39. 79 10 ATOM 1626 CA GLU 242 22.426 32. 440 35.017 1. 00 38. 35 1627 ATOM CBGLU 242 23. 841 32. 438 34. 435 1. 00 41. 38 ATOM 1628 CG GLU 242 24. 874 33.080 35. 345 1. 00 43. 21 1629 ATOM CD GLU 242 26.062 33. 639 34. 588 1. 00 46. 65 ATOM 1630 0E1 GLU 242 26. 489 33.026 33. 581 1.00 46.29 15 ATOM 1631 OE2 GLU 242 26. 581 34. 694 35. 014 1. 00 49. 23 ATOM 1632 C GLU 242 21.495 31.626 34. 144 1. 00 34. 71 ATOM 1633 0 GLU 242 21. 135 32. 057 33. 054 1. 00 33. 08 ATOM 1634 N LEU 243 21.085 30. 456 34. 612 1. 00 31. 90 ATOM 1635 CA LEU 243 20. 194 29. 652 33. 794 1. 00 30. 72 20 ATOM 1636 CB LEU 243 20. 125 28. 214 34. 285 1. 00 29. 40 ATOM 1637 CG LEU 243 21. 244 27. 279 1. 00 28. 38 33. 833 ATOM 1638 CD1 LEU 243 21. 264 27. 192 32. 321 1. 00 23. 84 ATOM 1639 CD2 LEU 243 22. 570 27. 786 34. 381 1. 00 31. 28 ATOM 1640 C LEU 243 18. 799 30. 222 33. 763 1. 00 31. 18 ATOM 1641 LEU 243 25 0 18. 143 30. 153 32. 729 1. 00 32. 86 ATOM 1642 VAL 244 18.350 30.779 N 34. 887 1. 00 30. 11 ATOM 1643 CA VAL 244 17. 011 31. 361 34. 979 1. 00 30. 23 ATOM 1644 CBVAL 244 16. 549 31. 527 36. 432 1. 00 31. 77 ATOM 1645 CG1 VAL 244 15. 085 31. 981 36. 444 1. 00 31. 84

- 201 -ATOM CG2 VAL 244 1646 16. 748 30. 234 37. 213 1. 00 31. 59 ATOM 1647 VAL 244 C 16. 955 32. 746 34. 361 1. 00 30. 94 ATOM 1648 0 VAL 244 17. 919 33. 499 34. 458 1. 00 31. 77 **ATOM** 1649 GLU 245 N 15. 819 33.083 33. 753 1. 00 32. 44 ATOM 1650 CA GLU 245 15. 625 34. 389 33. 125 1. 00 36. 05 1651 CBATOM GLU 245 14. 384 34. 384 32. 237 1. 00 35. 98 ATOM 1652 CG GLU 245 14. 542 35. 203 30. 981 1. 00 38. 72 ATOM 1653 CD GLU 245 15. 357 34. 449 29. 959 1. 00 41. 52 ATOM 1654 0E1 GLU 245 15.957 33. 428 30.356 1. 00 40. 02 10 ATOM 1655 OE2 GLU 245 15. 402 34. 859 28.776 1. 00 43. 26 1656 C ATOM GLU 245 15. 453 35. 511 34. 149 1. 00 39. 49 1657 0 ATOM GLU 245 15. 995 36.603 33. 978 1. 00 39. 69 ATOM 1658 14.676 N **GLY 246** 35. 239 35. 197 1. 00 42. 62 ATOM 1659 CA **GLY 246** 14. 417 36. 228 36. 233 1. 00 44. 14 15. 642 ATOM 1660 15 C GLY 246 36. 762 36. 953 1. 00 44. 54 ATOM 1661 0 GLY 246 16. 720 36. 163 36. 906 1. 00 43. 59 1662 ATOM N ASP 247 15. 476 37.896 37. 627 1. 00 44. 51 ATOM 1663 CA ASP 247 16. 582 38. 500 38. 345 1. 00 45. 26 1664 ATOM CBASP 247 17. 179 37. 540 39. 654 1. 00 48. 06 20 **ATOM** 1665 CG ASP 247 18. 102 39. 173 36. 436 1. 00 52. 60 **ATOM** 1666 OD1 ASP 247 19.016 38. 376 36. 744 1. 00 54. 76 **ATOM** 1667 OD2 ASP 247 17. 923 39. 584 35. 265 1. 00 54. 15 ATOM 1668 C ASP 247 16. 213 38. 993 39. 720 1. 00 44. 83 ATOM 1669 0 17.087 ASP 247 39.306 40. 518 1. 00 45. 80 1670 N ATOM GLU 248 14.930 25 39.064 40. 022 1. 00 44. 56 ATOM 1671 CA GLU 248 14. 561 39. 546 41. 336 1. 00 45. 70 ATOM 1672 CB GLU 248 13. 610 40. 727 41. 206 1. 00 50. 66 ATOM 1673 CG GLU 248 12. 441 40. 458 40. 298 1. 00 60. 84 ATOM 1674 CD GLU 248 11. 394 41.556 40. 355 1. 00 67. 29

0

- 202 -ATOM 1675 0E1 GLU 248 10. 742 41. 702 41. 414 1.00 69.90 0E2 GLU 248 ATOM 42. 273 39. 340 1. 00 71. 41 1676 11. 223 13. 952 38. 482 42. 224 1. 00 43. 15 ATOM 1677 C GLU 248 1. 00 42. 29 GLU 248 12. 986 37. 827 41. 855 ATOM 1678 0 38. 315 1. 00 42. 35 1679 N **GLY 249** 14. 530 43. 404 5 ATOM ATOM 1680 CA **GLY 249** 14. 023 37. 327 44. 330 1. 00 42. 91 36. 247 44. 625 1.00 43.93 ATOM 1681 C GLY 249 15. 044 1682 0 **GLY 249** 16. 177 36. 294 44. 145 1. 00 43. 62 ATOM 1683 ARG 250 14. 644 35. 267 45. 427 1. 00 43. 38 ATOM N **ATOM** 1684 CA ARG 250 15. 526 34. 160 45. 781 1.00 41.04 10 **ATOM** 1685 CB ARG 250 15. 819 34. 207 47. 293 1. 00 42. 27 1686 ARG 250 14. 745 34. 934 48. 114 1. 00 46. 82 ATOM CG 15. 139 49. 584 1.00 51.21 ATOM 1687 CD ARG 250 35. 142 ATOM 1688 NE ARG 250 16. 425 35. 828 49. 730 1.00 55.52 16. 864 36. 394 50. 855 1. 00 55. 63 ATOM 1689 CZARG 250 15 1690 NH1 ARG 250 16. 121 36. 375 51. 956 1. 00 55. 05 ATOM NH2 ARG 250 18.063 36. 962 50. 885 1. 00 54. 32 ATOM 1691 ATOM 1692 C ARG 250 14. 905 32. 812 45. 359 1. 00 38. 25 13. 681 32. 640 45. 394 ATOM 1693 0 ARG 250 1. 00 37. 44 **ATOM** 1694 N MET 251 15. 760 31.880 44. 932 1. 00 33. 58 20 **ATOM** 1695 CA MET 251 15. 352 30. 543 44. 492 1. 00 29. 34 ATOM 1696 CBMET 251 15. 326 30. 471 42. 966 1.00 24.54 1.00 17.89 15. 180 29.069 ATOM 1697 CG MET 251 42. 379 **ATOM** 1698 SD MET 251 14. 994 29. 090 40. 552 1. 00 18. 23 16.329 **ATOM** 1699 MET 251 28.087 40.075 1. 00 12. 48 CE 25 **ATOM** 1700 C MET 251 16.316 29. 481 45. 004 1. 00 30. 48 ATOM 1701 0 MET 251 17. 529 29. 640 44. 895 1. 00 31. 49 ATOM 1702 CYS 252 15. 775 28. 392 45. 546 1. 00 29. 56 N CYS 252 1. 00 26. 54 ATOM 1703 CA 16. 599 27. 298 46.059

- 203 -1. 00 27. 29 ATOM 1704 CBCYS 252 15. 710 26. 185 46. 612 1. 00 29. 14 24. 659 46. 927 ATOM 1705 SG CYS 252 16. 613 1. 00 23. 38 CYS 252 26. 704 44. 975 ATOM 1706 C 17. 492 1. 00 22. 79 CYS 252 17. 104 26. 639 43. 816 ATOM 1707 0 45. 349 1. 00 20. 80 VAL 253 18.688 26. 268 **ATOM** 1708 N 5 VAL 253 19. 584 25. 660 44. 377 1. 00 20. 25 ATOM 1709 CA 1710 CB VAL 253 20. 740 26. 583 43. 969 1. 00 19. 02 ATOM 1. 00 15. 42 CG1 VAL 253 21. 623 25. 881 42. 936 ATOM 1711 CG2 VAL 253 27. 866 43. 411 1. 00 19. 77 ATOM 1712 20. 198 44. 900 1. 00 22. 35 1713 C VAL 253 20. 191 24. 374 **ATOM** 10 VAL 253 20.705 24. 305 46. 023 1. 00 22. 21 **ATOM** 1714 0 20. 127 23. 352 44.060 1. 00 24. 23 ATOM 1715 N ASN 254 20.661 22. 045 44. 390 1. 00 22. 10 ATOM 1716 CA ASN 254 1. 00 21. 49 ASN 254 19.860 20. 975 43. 647 ATOM 1717 CB 20. 479 19.604 43. 747 1. 00 22. 93 ATOM 1718 CG ASN 254 15 21.074 19. 232 44. 764 1. 00 20. 03 1719 OD1 ASN 254 ATOM 20. 325 18. 827 42. 687 1. 00 26. 40 **ATOM** 1720 ND2 ASN 254 22. 046 1721 22. 124 43. 975 1. 00 19. 26 C ASN 254 ATOM 1722 22. 454 22. 155 42. 795 1. 00 15. 88 ATOM 0 ASN 254 21. 949 1723 23. 001 44. 961 1. 00 15. 23 ATOM N THR 255 20 1724 THR 255 24. 428 21. 962 44. 691 1. 00 15. 03 ATOM CA 25. 193 22. 217 45. 944 1. 00 13. 56 1725 CB THR 255 ATOM 1726 OG1 THR 255 25. 035 21. 087 46. 808 1. 00 14. 56 ATOM CG2 THR 255 24. 670 23. 458 46. 617 1. 00 14. 18 ATOM 172724.957 20.665 44. 127 1. 00 15. 21 ATOM 1728 C THR 255 25 1. 00 12. 07 THR 255 25.675 20. 647 43. 126 ATOM 1729 0 24. 594 19. 570 44. 777 1. 00 18. 83 **ATOM** 1730 N **GLU 256** 18. 268 44. 355 1. 00 22. 28 1731 GLU 256 25. 076 ATOM CA 42. 876 1732 CB 24. 795 18. 025 1. 00 25. 93 ATOM GLU 256

- 204 -ATOM 1733 CG GLU 256 23. 377 18. 345 42. 454 1.00 31.90 ATOM 1734 CD GLU 256 22. 500 17. 121 42. 336 1. 00 34. 74 ATOM OE1 GLU 256 1735 22. 191 16. 510 43. 386 1. 00 36. 97 ATOM 1736 OE2 GLU 256 22. 122 16. 777 41. 188 1. 00 35. 26 5 ATOM 1737 C GLU 256 26. 562 18. 402 44. 559 1. 00 21. 32 ATOM 1738 0 GLU 256 27. 359 18. 032 43. 701 1. 00 23. 09 ATOM 1739 N TRP 257 26. 931 18. 966 45.699 1. 00 17. 36 ATOM 1740 CA TRP 257 28. 327 19. 141 45. 985 1.00 14.83 ATOM 1741 CB TRP 257 28. 514 20. 074 47. 176 1.00 11.59 ATOM 10 1742 CG TRP 257 28. 038 19. 561 48. 478 1.00 8.69 ATOM 1743 CD2 TRP 257 27.830 20. 332 49.676 1. 00 9.05 ATOM 1744 CE2 TRP 257 27. 562 19. 410 50. 715 1. 00 7.00 ATOM CE3 TRP 257 1745 27. 845 21. 703 49. 964 1. 00 7. 18 ATOM 1746 CD1 TRP 257 27.881 18. 265 48. 827 1.00 7. 58 15 ATOM 1747 NE1 TRP 257 27.602 18. 163 50. 172 1.00 7.99 ATOM 1748 CZ2 TRP 257 27. 325 19.818 52. 038 1.00 4. 73 ATOM CZ3 TRP 257 1749 27.605 22. 108 51. 280 1.00 7. 12 **ATOM** 1750 CH2 TRP 257 27. 346 21. 164 52. 300 1.00 5.47 ATOM 1751 C TRP 257 29.033 17. 813 46. 224 1. 00 17. 81 ATOM 20 1752 0 TRP 257 30. 221 17. 776 46. 523 1.00 19.44 ATOM 1753 N GLY 258 28. 318 16. 708 46. 099 1. 00 21. 88 **ATOM** 1754 CA GLY 258 28. 991 15. 444 46. 303 1. 00 23. 25 ATOM 1755 C **GLY 258** 30. 137 15. 303 45. 316 1. 00 23. 01 ATOM 1756 0 GLY 258 31. 133 14. 629 45.600 1. 00 21. 92 **ATOM** 25 1757 N ALA 259 29. 997 15. 943 44. 156 1. 00 23. 11 **ATOM** 1758 CA ALA 259 31. 015 15. 863 43. 113 1. 00 27. 74 ATOM 1759 CBALA 259 30. 400 16. 139 41.766 1. 00 27. 03 ATOM 1760 C ALA 259 32. 176 16.806 43. 335 1. 00 30. 23 **ATOM** 1761 0 ALA 259 33. 178 16. 748 42. 622 1. 00 32. 12

- 205 -ATOM 1762 PHE 260 N 32. 041 17. 680 44. 320 1. 00 32. 43 **ATOM** 1763 CA PHE 260 33.093 18. 627 44. 611 1.00 36.43 ATOM 1764 CBPHE 260 32.804 19. 343 45. 924 1.00 39.42 ATOM 1765 CG PHE 260 33. 932 20. 206 46. 411 1.00 43.92 ATOM 1766 CD1 PHE 260 5 34.660 21.003 45. 534 1.00 46.49 ATOM 1767 CD2 PHE 260 34. 232 20. 263 47. 765 1.00 45.64 ATOM 1768 CE1 PHE 260 35. 672 21. 835 46. 002 1.00 47.73 CE2 PHE 260 ATOM 1769 35. 242 21. 093 48. 242 1.00 46.62 ATOM 1770 CZPHE 260 35. 958 21.882 47. 360 1.00 47.27 ATOM 1771 C PHE 260 10 34. 412 17. 897 44. 695 1.00 39.39 ATOM 1772 0 PHE 260 34. 495 16.800 45. 243 1.00 40.20 ATOM 1773 N GLY 261 35. 441 18. 511 44. 127 1.00 41.71 ATOM 1774 CA GLY 261 36. 753 17. 911 44. 152 1.00 43.62 ATOM 1775 C GLY 261 36. 967 16.857 43.090 1.00 44.99 ATOM 1776 0 GLY 261 15 38. 049 16. 282 43. 015 1. 00 47. 22 ATOM 1777 N ASP 262 35.961 16. 578 42. 270 1.00 46.06 ATOM 1778 CA ASP 262 36. 143 15. 574 41. 229 1.00 47.68 ATOM 1779 CBASP 262 34. 800 15. 197 40.602 1.00 50.82 ATOM 1780 CG ASP 262 34. 024 14. 187 41. 445 1. 00 53. 64 ATOM 20 1781 OD1 ASP 262 32.815 13. 996 41. 191 1.00 54.63 ATOM 1782 OD2 ASP 262 34.624 13. 578 42. 356 1.00 54.71 ATOM 1783 C ASP 262 37. 089 16. 129 40. 177 1.00 47.19 37. 539 ATOM 1784 0 ASP 262 15. 400 39. 292 1.00 47.09 ATOM 1785 N SER 263 37. 380 17. 427 40. 298 1.00 46.38 25 ATOM 1786 CA SER 263 38. 289 18. 147 39. 401 1.00 44.53 ATOM 1787 CB SER 263 37. 651 19. 445 38. 903 1.00 43.57 ATOM 1788 SER 263 0G 36. 341 19. 246 38. 415 1.00 43.79 ATOM 1789 C SER 263 39. 552 18. 513 40. 174 1. 00 43. 93 ATOM 1790 0 SER 263 40.061 19.632 40. 059 1.00 44.40

- 206 -1.00 43.71 GLY 264 40.039 17. 577 40. 979 **ATOM** 1791 N 1.00 42.64 41. 762 ATOM 1792 CA GLY 264 41. 235 17. 825 1. 00 40. 75 18. 889 42. 845 GLY 264 41. 133 ATOM 1793 C 1. 00 42. 90 **GLY 264** 42.052 19. 012 43. 648 ATOM 1794 0 42. 887 1. 00 38. 43 40.040 19.647 GLU 265 ATOM 1795 N 5 39.881 20.700 43.893 1.00 37.42 GLU 265 **ATOM** 1796 CA **GLU 265** 38. 437 21. 227 43. 907 1. 00 39. 11 **ATOM** 1797 CB 1. 00 40. 76 37. 986 21. 928 42. 632 GLU 265 ATOM 1798 CG 21.023 41.701 1.00 43.56 CD GLU 265 37. 198 ATOM 1799 1.00 45.26 21.461 40.565 OE1 GLU 265 36. 904 ATOM 1800 10 19.883 42.099 1. 00 42. 42 1801 0E2 GLU 265 36.863 ATOM 1. 00 36. 38 20. 299 45. 321 **GLU 265** 40. 266 ATOM 1802 C 46. 185 1. 00 33. 59 **ATOM** 1803 0 GLU 265 40. 410 21. 160 1.00 37.71 19.004 45. 573 N LEU 266 40. 425 **ATOM** 1804 18. 534 46.912 1. 00 40. 56 **ATOM** 1805 CA LEU 266 40. 783 15 17. 831 47. 567 1. 00 40. 03 LEU 266 39. 597 **ATOM** 1806 CB48.001 1. 00 40. 79 CG LEU 266 38. 371 18. 631 ATOM 1807 37. 234 17. 673 48. 259 1. 00 40. 27 CD1 LEU 266 **ATOM** 1808 38. 677 19. 432 49. 253 1. 00 41. 81 ATOM 1809 CD2 LEU 266 41.949 17. 563 46. 880 1. 00 43. 51 20 ATOM 1810 C LEU 266 17.045 47. 919 1.00 43.63 1811 0 LEU 266 42. 363 ATOM 17. 324 45.682 1. 00 47. 00 ASP 267 42. 475 1812 N ATOM ASP 267 43. 584 16. 393 45. 480 1. 00 48. 18 **ATOM** 1813 CA44. 222 16. 622 44.097 1. 00 50. 89 ASP 267 ATOM 1814 CB 1. 00 54. 98 1815 CG ASP 267 44. 982 15. 391 43. 584 ATOM 25 1. 00 56. 65 45. 239 15. 317 42.360 1816 OD1 ASP 267 ATOM 44. 398 1. 00 55. 43 OD2 ASP 267 45. 328 14. 499 **ATOM** 1817 ASP 267 44.659 46. 571 1. 00 46. 46 **ATOM** 1818 С 16. 440 45. 205 46.960 1. 00 45. 37 1819 ASP 267 15. 397 ATOM 0

- 207 -**ATOM** 1820 N GLU 268 44. 957 17. 630 47. 084 1. 00 44. 63 1821 **GLU 268** 45. 990 17. 721 48. 109 1. 00 44. 67 ATOM CA 1822 GLU 268 46.805 19. 024 47. 956 1. 00 44. 68 ATOM CB 1823 GLU 268 46. 508 20. 163 48. 934 1. 00 43. 60 ATOM CG 1824 GLU 268 45. 234 20. 915 48. 613 1. 00 43. 53 5 ATOM CD ATOM 1825 0E1 GLU 268 45.020 21. 258 47. 423 1. 00 42. 43 0E2 GLU 268 44. 461 21. 174 49. 561 ATOM 1826 1. 00 40. 84 ATOM 1827 C GLU 268 45. 457 17. 569 49. 528 1. 00 43. 45 1828 ATOM **GLU 268** 46. 102 17. 961 50. 499 1. 00 46. 29 0 ATOM 1829 N PHE 269 44. 286 16. 971 49.656 1. 00 38. 78 10 16. 785 ATOM 1830 CA PHE 269 43. 729 50. 974 1. 00 33. 75 1831 PHE 269 42. 480 17. 614 51. 135 1. 00 33. 69 ATOM CB 1832 PHE 269 42. 733 18. 990 1. 00 34. 75 ATOM CG 51. 639 **ATOM** 1833 CD1 PHE 269 43. 435 19. 193 52. 822 1. 00 36. 51 CD2 PHE 269 ATOM 1834 42. 161 20.079 51.001 1. 00 34. 78 15 1835 CE1 PHE 269 43.548 20. 469 53. 365 ATOM 1. 00 37. 39 21. 354 ATOM 1836 CE2 PHE 269 42. 266 51. 532 1. 00 35. 15 ATOM 1837 CZPHE 269 42. 955 21. 551 52. 717 1. 00 37. 68 15. 343 51. 225 ATOM 1838 C PHE 269 43. 405 1. 00 32. 83 ATOM 1839 PHE 269 43. 206 14. 952 52. 365 20 0 1. 00 31. 85 ATOM 1840 N LEU 270 43. 355 14. 555 50. 157 1. 00 33. 85 ATOM 1841 CA LEU 270 43.046 13. 130 50. 259 1. 00 34. 53 ATOM 1842 CB LEU 270 42. 712 12. 553 48. 884 1. 00 35. 63 LEU 270 41. 326 12. 857 **ATOM** 1843 CG 48. 321 1. 00 37. 61 41. 323 ATOM 1844 CD1 LEU 270 14. 293 47. 842 1. 00 35. 85 25 **ATOM** CD2 LEU 270 40.966 11.878 1. 00 37. 50 1845 47. 177 **ATOM** 1846 C LEU 270 44. 172 12. 298 50.845 1. 00 33. 68 1.00 35.64 ATOM 1847 LEU 270 45. 334 12. 640 0 50. 695 ATOM 1848 N LEU 271 43. 829 11. 200 51. 507 1. 00 33. 66

- 208 -ATOM 1849 CA LEU 271 44. 850 10. 324 52. 059 1. 00 34. 55 10. 032 53. 519 1. 00 30. 63 ATOM 1850 CB LEU 271 44. 610 CG LEU 271 44.870 11. 238 54. 383 1. 00 29. 49 ATOM 1851 1852 CD1 LEU 271 43.855 12. 324 54. 075 1. 00 27. 82 ATOM CD2 LEU 271 1853 44. 783 10. 798 55. 824 1.00 31.04 5 ATOM ATOM 1854 C LEU 271 44.884 9. 010 51. 324 1.00 37.04 ATOM 1855 0 LEU 271 44.009 8. 715 50. 513 1. 00 36. 79 ATOM 1856 N GLU 272 45. 890 8. 209 51. 638 1. 00 40. 66 **ATOM** 1857 CA GLU 272 46.052 6. 927 50.989 1. 00 44. 99 **ATOM** 1858 CB **GLU 272** 47. 256 6. 182 51. 590 1. 00 51. 18 10 ATOM 1859 CG GLU 272 47. 124 5. 781 53. 075 1. 00 58. 46 1860 CDGLU 272 48. 371 5. 077 53. 641 1. 00 62. 56 ATOM 1861 OE1 GLU 272 49.393 5. 772 53.876 1.00 64.96 ATOM ATOM 1862 0E2 GLU 272 48. 325 3.835 53. 849 1.00 61.73 ATOM 1863 C GLU 272 44. 789 6.080 51. 092 1. 00 44. 62 15 1864 0 GLU 272 44. 377 5. 452 50. 116 1. 00 44. 50 ATOM ATOM 1865 TYR 273 44. 163 6.079 52. 266 1. 00 43. 42 N ATOM 1866 CA TYR 273 42. 955 5. 284 52. 486 1. 00 40. 23 1867 TYR 273 42. 537 5. 377 53. 958 1. 00 38. 82 ATOM CB ATOM 1868 CG TYR 273 43.709 5. 401 54. 923 1. 00 36. 38 20 CD1 TYR 273 ATOM 1869 44. 126 6.602 55. 505 1. 00 35. 57 ATOM 1870 CE1 TYR 273 45. 210 6.647 56. 380 1. 00 34. 95 1. 00 35. 34 1871 CD2 TYR 273 4. 231 ATOM 44. 413 55. 243 ATOM 1872 CE2 TYR 273 45. 509 4. 264 56. 122 1. 00 34. 05 ATOM 1873 CZ TYR 273 45. 897 5. 481 56. 685 1. 00 34. 66 25 **ATOM** 1874 0HTYR 273 46.966 5. 556 57. 550 1. 00 33. 77 ATOM 1875 C TYR 273 41.826 5. 749 51. 567 1. 00 38. 50 ATOM 1876 TYR 273 41. 264 4. 967 1. 00 35. 21 0 50. 804 ATOM 1877 N ASP 274 41. 507 7. 030 51. 638 1. 00 38. 17

- 209 -CA ASP 274 40. 473 7. 579 50. 796 1. 00 40. 03 **ATOM** 1878 9.083 50. 929 1.00 41.17 ATOM 1879 CBASP 274 40. 470 1.00 43.77 9. 512 52. 341 ASP 274 40. 252 ATOM 1880 CG 9. 327 52.839 1. 00 46. 59 OD1 ASP 274 39. 123 ATOM 1881 10.010 52.958 1.00 44.41 41. 212 ATOM 1882 OD2 ASP 274 5 ASP 274 40.740 7. 200 49. 359 1. 00 40. 92 **ATOM** 1883 C 1.00 41.41 ASP 274 39.819 6. 937 48. 595 **ATOM** 1884 0 1. 00 42. 93 42.007 7. 160 48. 984 1885 N ARG 275 ATOM 6.819 47. 613 1. 00 45. 81 ATOM 1886 CA ARG 275 42. 333 6.993 1.00 49.53 47. 365 CBARG 275 43.831 ATOM 1887 10 7. 563 45. 995 1. 00 53. 24 **ATOM** 1888 CG ARG 275 44. 191 1. 00 58. 85 7. 772 45. 886 1889 CD ARG 275 45. 702 ATOM 8.663 46. 933 1. 00 62. 67 **ATOM** 1890 NE ARG 275 46. 213 8.308 1. 00 62. 82 47.088 47. 876 ATOM 1891 CZARG 275 47. 571 7.068 47. 922 1. 00 61. 28 ATOM 1892 NH1 ARG 275 15 9. 201 48. 777 1.00 61.64 1893 NH2 ARG 275 47. 476 ATOM 41. 901 5. 390 47. 316 1.00 46.01 ATOM 1894 C ARG 275 41. 134 5. 160 1.00 45.19 1895 ARG 275 46. 382 0 ATOM 1. 00 47. 51 42. 382 4. 437 48. 113 ATOM 1896 N LEU 276 1. 00 48. 68 42. 026 3. 030 47. 922 1897 LEU 276 20 ATOM CA 2. 197 49. 134 1. 00 45. 63 1898 CB LEU 276 42. 460 ATOM 1.999 49. 287 1. 00 43. 28 LEU 276 43. 971 1899 CG ATOM CD1 LEU 276 44. 418 2. 379 50. 686 1. 00 42. 53 ATOM 1900 44. 321 0. 557 48. 994 1. 00 42. 97 1901 CD2 LEU 276 ATOM 2. 915 47.718 1. 00 51. 24 ATOM 1902 C LEU 276 40. 520 25 1. 00 52. 38 40.050 2. 133 46. 891 1903 LEU 276 ATOM 0 3.710 48. 475 1. 00 53. 11 ATOM 1904 N VAL 277 39. 772 3. 722 48. 372 1. 00 54. 05 VAL 277 38. 321 ATOM 1905 CA CB37. 703 4.640 49. 423 1. 00 52. 84 ATOM 1906 VAL 277

- 210 -1. 00 52. 71 ATOM 1907 CG1 VAL 277 36. 210 4. 682 49. 249 1908 ATOM CG2 VAL 277 38.069 4. 156 50.804 1. 00 54. 87 **ATOM** C VAL 277 37. 906 4. 231 46. 999 1. 00 55. 80 1909 VAL 277 3.474 46. 185 1. 00 57. 15 **ATOM** 1910 0 37. 381 ASP 278 5.518 46.754 1.00 56.71 ATOM 1911 N 38. 146 5 ATOM 1912 CA ASP 278 37.804 6. 146 45. 481 1. 00 57. 65 ATOM CBASP 278 38. 479 7.514 45. 353 1. 00 59. 73 1913 ASP 278 ATOM 1914 CG 38. 243 8. 163 43. 989 1. 00 61. 93 **ATOM** 1915 OD1 ASP 278 38.990 9. 110 43. 642 1. 00 61. 47 ATOM 1916 OD2 ASP 278 37. 308 7. 733 43. 273 1. 00 62. 11 10 ASP 278 5. 281 1. 00 58. 14 ATOM 1917 C 38. 263 44. 328 ATOM 1918 0 ASP 278 37. 645 5. 271 43. 266 1. 00 58. 75 ATOM 1919 N GLU 279 39. 358 4. 563 44. 538 1. 00 58. 33 **ATOM** 1920 CA GLU 279 39.900 3.710 43. 498 1. 00 59. 14 ATOM 1921 CBGLU 279 41. 437 3. 808 43. 477 1. 00 60. 99 15 ATOM 1922 CG GLU 279 41. 978 5. 219 43. 178 1. 00 61. 92 1923 CD GLU 279 43. 497 5. 276 43.014 1. 00 60. 92 ATOM ATOM 1924 0E1 GLU 279 44. 219 4.874 43. 953 1. 00 60. 85 1925 0E2 GLU 279 43.965 5. 733 41. 946 1. 00 58. 99 ATOM ATOM 1926 C **GLU 279** 39. 467 2. 261 43.664 1.00 58.04 20 GLU 279 40. 196 1. 346 ATOM 1927 0 43. 298 1. 00 59. 38 ATOM 1928 N SER 280 38. 283 2. 044 44. 219 1. 00 57. 21 1929 SER 280 37. 798 0.679 44. 390 1. 00 56. 55 ATOM CA ATOM 1930 CB SER 280 38. 283 0.091 45. 719 1. 00 56. 66 -1.2981931 SER 280 38.015 45. 774 1. 00 54. 41 25 ATOM 0G ATOM 1932 С SER 280 36. 282 0.671 44. 334 1. 00 55. 29 -0.371ATOM 1933 0 SER 280 35. 640 44. 472 1. 00 53. 68 1934 N SER 281 35. 725 1. 854 44. 113 1. 00 54. 58 ATOM ATOM 1935 CA SER 281 34. 288 2. 038 44. 020 1. 00 55. 36

- 211 -**ATOM** 1936 CBSER 281 33. 919 3. 451 44. 464 1. 00 56. 89 ATOM 1937 0G SER 281 34. 565 4. 415 43. 649 1. 00 56. 89 ATOM 1938 C SER 281 33. 843 1. 832 42. 584 1. 00 54. 80 ATOM 1939 0 SER 281 34. 652 1. 905 41.664 1. 00 55. 85 5 ATOM 1940 N ALA 282 32. 553 1. 587 42. 389 1. 00 53. 75 ATOM 1941 CA ALA 282 32. 025 1. 379 41.050 1. 00 52. 42 ATOM 1942 CBALA 282 30.626 0.809 41. 133 1. 00 52. 26 ATOM 1943 C ALA 282 32. 012 2.679 40. 250 1.00 51.83 ATOM 1944 0 ALA 282 31. 632 2. 685 39.081 1. 00 52. 27 10 ATOM 1945 N ASN 283 32. 441 3. 772 40.879 1. 00 50. 19 ATOM 1946 CA ASN 283 32. 465 5. 089 40. 239 1. 00 47. 37 ATOM 1947 CB ASN 283 31. 338 5. 945 40.790 1. 00 47. 04 **ATOM** 1948 CG ASN 283 31. 482 6. 191 42. 276 1. 00 47. 38 **ATOM** 1949 OD1 ASN 283 31.584 5. 255 43.068 1. 00 46. 86 15 ATOM 1950 ND2 ASN 283 31. 497 7. 455 42. 662 1. 00 49. 96 **ATOM** 1951 C ASN 283 33. 777 5.806 40. 513 1.00 46.64 ATOM 1952 0 ASN 283 33. 783 6. 894 41.081 1. 00 48. 74 ATOM 1953 N PRO 284 34. 905 5. 214 40. 110 1. 00 45. 15 **ATOM** 1954 PRO 284 CD 35.028 3.896 39. 462 1. 00 44. 41 ATOM 20 1955 PRO 284 CA 36. 227 5.814 40. 327 1. 00 43. 24 ATOM 1956 CB PRO 284 37. 151 4. 855 39. 583 1.00 44.66 **ATOM** 1957 CG PRO 284 36. 459 3. 532 39. 756 1. 00 44. 93 ATOM 1958 C PRO 284 36. 389 7. 267 39. 856 1. 00 41. 14 ATOM 1959 0 PRO 284 35. 978 7.624 38. 755 1. 00 40. 17 25 ATOM 1960 N GLY 285 36. 994 8. 099 40.695 1. 00 39. 45 **ATOM** 1961 CA GLY 285 37. 208 9. 484 40. 321 1. 00 40. 34 ATOM 1962 C GLY 285 35. 964 10. 343 40.401 1.00 42.06 ATOM 1963 GLY 285 0 36. 035 11. 576 40.367 1. 00 43. 11 ATOM 1964 N GLN 286 34. 811 9. 699 40. 510 1. 00 42. 34

- 212 -ATOM 1965 CA GLN 286 33. 555 10. 427 40.601 1. 00 41. 88 ATOM 1966 CBGLN 286 32. 490 9. 717 39. 758 1. 00 44. 97 ATOM 1967 CG GLN 286 31. 973 10. 544 38. 588 1. 00 49. 89 **ATOM** 1968 CD **GLN 286** 31.043 11.668 1. 00 54. 72 39. 043 ATOM 1969 OE1 GLN 286 29. 911 11. 419 39. 483 1.00 56.09 5 NE2 GLN 286 12. 911 1.00 54.20 ATOM 1970 31. 519 38. 950 1971 C **GLN 286** 10. 541 42.063 1.00 40.59 ATOM 33. 113 1972 **GLN 286** 33. 396 9.660 1.00 39.39 ATOM 0 42. 879 **ATOM** 1973 **GLN 287** 11. 648 42. 389 1.00 39.59 N 32. 445 10 ATOM 1974 CA GLN 287 31. 939 11. 913 43. 741 1.00 38.06 ATOM GLN 287 30.770 10.969 1. 00 37. 29 1975 CB 44. 053 ATOM 1976 CG GLN 287 29. 732 10. 837 42. 939 1. 00 35. 04 28.912 **ATOM** 1977 CD GLN 287 12. 100 42. 736 1. 00 33. 74 ATOM 1978 0E1 GLN 287 28. 906 12.692 41.647 1. 00 28. 89 ATOM 1979 NE2 GLN 287 28. 204 12. 514 43. 786 1.00 31.49 15 ATOM 1980 C GLN 287 33. 015 11. 744 44. 820 1. 00 37. 30 1981 GLN 287 32.958 10.813 ATOM 0 45. 624 1. 00 37. 53 ATOM 1982 N LEU 288 33. 990 12.643 44.856 1.00 34.03 1983 35.051 ATOM CA LEU 288 12. 516 45. 844 1. 00 29. 84 1984 36. 351 20 ATOM CB LEU 288 13. 071 45. 293 1. 00 30. 50 ATOM 1985 CG LEU 288 37. 285 11. 960 44.819 1. 00 32. 69 ATOM 1986 CD1 LEU 288 36.645 11. 102 43. 728 1. 00 31. 90 CD2 LEU 288 **ATOM** 1987 38. 546 12. 611 44. 323 1.00 36.00 ATOM 1988 C LEU 288 34. 729 13. 180 47. 156 1. 00 26. 53 1989 LEU 288 34.991 12.627 ATOM 0 48. 218 1. 00 26. 76 25 ATOM 1990 N TYR 289 34. 172 14. 374 47. 086 1. 00 23. 58 1991 TYR 289 33. 809 ATOM CA 15. 074 48. 292 1. 00 22. 36 ATOM 1992 CB TYR 289 33. 086 16. 365 47. 939 1. 00 20. 16 **ATOM** 1993 CG TYR 289 32. 716 17. 186 49. 136 1. 00 18. 61

- 213 -ATOM 1994 CD1 TYR 289 33. 660 17. 486 50. 105 1. 00 18. 65 ATOM 1995 CE1 TYR 289 33. 347 18. 269 51. 195 1.00 18.34 ATOM 1996 CD2 TYR 289 31. 433 17. 693 49. 288 1. 00 18. 91 ATOM 1997 CE2 TYR 289 31. 105 18. 484 50. 378 1. 00 18. 97 ATOM 1998 CZ TYR 289 32.073 18.768 5 51. 327 1. 00 20. 15 ATOM 1999 0HTYR 289 31.788 19.565 52. 408 1. 00 22. 93 2000 ATOM C TYR 289 32. 894 14. 165 49. 105 1. 00 25. 30 ATOM 2001 0 TYR 289 32. 991 14. 106 50. 337 1. 00 24. 21 ATOM 2002 GLU 290 N 32.005 13. 448 48. 411 1. 00 27. 35 10 ATOM 2003 CA GLU 290 31.071 12. 532 49.084 1. 00 26. 68 ATOM 2004 CBGLU 290 30.081 11. 904 48.090 1. 00 26. 17 ATOM 2005 CG GLU 290 28. 614 12. 216 48. 413 1. 00 25. 68 ATOM 2006 CD GLU 290 27. 617 11. 404 47. 591 1. 00 26. 93 ATOM 2007 0E1 GLU 290 27. 735 11. 363 46. 337 1. 00 22. 27 15 ATOM 2008 0E2 GLU 290 26. 702 10.815 48. 215 1. 00 27. 37 ATOM 2009 C GLU 290 31.838 11. 425 49. 781 1. 00 25. 75 ATOM 2010 0 GLU 290 31. 649 11. 193 50. 974 1. 00 26. 23 ATOM 2011 N LYS 291 32. 706 10.756 49. 024 1. 00 24. 16 ATOM 2012 LYS 291 CA 33. 526 9.666 49. 538 1. 00 24. 45 20 ATOM 2013 CB LYS 291 34. 342 9.063 48. 408 1. 00 24. 19 ATOM 2014 CG LYS 291 33.506 8. 383 47. 354 1. 00 28. 37 ATOM 2015 CDLYS 291 34. 322 8. 162 46.094 1. 00 31. 52 ATOM 2016 CE LYS 291 33. 533 7. 434 45. 030 1. 00 31. 16 ATOM LYS 291 34. 367 2017 NZ 7. 299 43. 813 1. 00 33. 55 **ATOM** LYS 291 25 2018 C 34.460 10. 143 50. 636 1. 00 24. 99 ATOM 2019 0 LYS 291 35. 488 9. 522 50. 918 1. 00 25. 78 ATOM 2020 N LEU 292 34.095 11. 254 51. 255 1. 00 24. 20 ATOM 2021 CA LEU 292 34. 894 11. 809 52. 318 1. 00 25. 20 ATOM 2022 CBLEU 292 1. 00 25. 62 35. 544 13. 106 51. 843

- 214 -2023 CG LEU 292 ATOM 36. 904 13. 450 52. 464 1.00 26.59 ATOM 2024 CD1 LEU 292 37. 935 12. 396 52. 035 1. 00 26. 37 2025 CD2 LEU 292 37. 343 14. 853 ATOM 52. 025 1.00 24.08 2026 C LEU 292 12.063 ATOM 33. 999 53. 528 1. 00 26. 58 ATOM 2027 0 LEU 292 34. 431 11. 924 54. 671 1.00 27.91 5 2028 ILE 293 ATOM N 32. 744 12. 421 53. 272 1.00 27.03 2029 ILE 293 31. 783 12. 689 ATOM CA 54. 342 1.00 26.01 2030 **ATOM** CB ILE 293 30. 948 13. 956 54. 019 1.00 26.42 ATOM 2031 CG2 ILE 293 30. 184 14. 431 55. 247 1. 00 25. 08 ATOM 2032 CG1 ILE 293 10 31. 866 15. 085 53. 573 1. 00 24. 53 CD1 ILE 293 **ATOM** 2033 31. 131 16. 366 53. 336 1. 00 23. 77 2034 C ILE 293 30.827 ATOM 11. 503 54. 489 1.00 24.65 2035 **ATOM** 0 ILE 293 30. 681 10. 919 55. 565 1.00 23.84 2036 ATOM N GLY 294 30. 197 11. 159 53. 374 1. 00 24. 02 2037 CA 29. 237 10.073 15 ATOM GLY 294 53. 325 1. 00 25. 49 ATOM 2038 C GLY 294 29. 454 8. 815 54. 142 1. 00 24. 75 2039 **ATOM** 0 **GLY 294** 30. 427 8.079 53.953 1. 00 26. 25 2040 ATOM N GLY 295 28. 517 8. 556 55. 044 1. 00 22. 54 **ATOM** 2041 CA **GLY 295** 28. 607 7. 369 55. 851 1. 00 22. 80 20 **ATOM** 2042 C GLY 295 28. 530 6. 125 54. 986 1. 00 25. 08 **ATOM** 2043 0 **GLY 295** 28. 252 5. 047 55. 497 1.00 27.80 ATOM 2044 N LYS 296 28. 748 6. 238 53. 680 1. 00 25. 43 ATOM 2045 LYS 296 28.696 5. 039 CA 52. 849 1. 00 25. 87 2046 ATOM CB LYS 296 28. 313 5. 354 51. 411 1.00 27.04 ATOM 2047 CG LYS 296 28. 036 4.096 25 50. 587 1. 00 30. 40 ATOM 2048 CD LYS 296 29. 249 3. 562 49. 842 1. 00 30. 20 ATOM 2049 CE LYS 296 28. 954 2. 204 49. 176 1. 00 32. 59 **ATOM** 2050 NZLYS 296 29. 015 1. 038 50. 135 1. 00 32. 31

ATOM

2051

C

LYS 296

30. 044

52. 828

4. 364

1.00 28.34

- 215 -1. 00 29. 08 ATOM 2052 0 LYS 296 30. 158 3. 185 52. 507 **ATOM** 2053 TYR 297 31.075 5. 122 53. 163 1. 00 29. 56 N ATOM CA TYR 297 32. 414 4.582 53. 147 1. 00 29. 25 2054 TYR 297 5. 230 52.022 1. 00 30. 07 ATOM 2055 CB 33. 208 TYR 297 5.025 50.650 1.00 30.84 **ATOM** 2056 CG 32.620 5 CD1 TYR 297 6.082 ATOM 2057 32. 023 49. 960 1. 00 32. 45 **ATOM** CE1 TYR 297 5.915 48.665 1. 00 35. 21 2058 31. 544 1.00 30.51 3.789 50.015 **ATOM** 2059 CD2 TYR 297 32. 715 **ATOM** CE2 TYR 297 3.604 48. 724 1. 00 34. 82 2060 32. 244 10 **ATOM** 2061 CZTYR 297 31.661 4.673 48.049 1. 00 37. 82 ATOM 0HTYR 297 31. 219 4. 504 46. 753 1. 00 41. 74 2062 ATOM 2063 C TYR 297 33.097 4. 842 54. 465 1.00 27.53 **ATOM** TYR 297 34. 174 4. 312 54. 731 1. 00 28. 35 2064 0 ATOM 2065 N MET 298 32. 464 5.665 55. 288 1. 00 24. 45 6.000 1.00 23.96 15 ATOM 2066 $\mathsf{C}\mathsf{A}$ MET 298 33. 025 56. 580 ATOM 2067 CB MET 298 31. 959 6.652 57. 454 1. 00 21. 69 2068 6. 992 ATOM CG MET 298 32. 436 58.850 1. 00 20. 73 **ATOM** 2069 SD MET 298 31. 288 8. 100 59.701 1.00 20.68 9. 523 ATOM 2070 CE MET 298 31. 435 58. 620 1. 00 18. 32 4. 750 20 ATOM 2071 C MET 298 33. 579 57. 254 1. 00 24. 25 ATOM 2072 0 MET 298 34. 776 4.656 57. 529 1.00 24.74 ATOM 2073 N **GLY 299** 32. 707 3. 779 57. 494 1. 00 26. 72 ATOM GLY 299 33. 135 2. 552 58. 135 1. 00 25. 77 2074 CA **ATOM** 2075 C **GLY 299** 34. 301 1. 906 57. 424 1. 00 25. 50 1.331 ATOM 2076 **GLY 299** 35. 162 58.076 1. 00 26. 16 25 0 **ATOM** 2077 N **GLU 300** 34. 325 2.004 56. 095 1. 00 25. 37 ATOM 2078 CA **GLU 300** 35. 389 1. 418 55. 282 1. 00 24. 57 CB 1.551 53.800 1. 00 24. 05 ATOM 2079 GLU 300 35. 057 CG ATOM 2080 **GLU 300** 36.066 0.859 52. 905 1. 00 24. 66

- 216 -ATOM CD GLU 300 36. 018 -0. 662 53. 004 1. 00 24. 52 2081 -1. 195 54. 054 1. 00 24. 02 OE1 GLU 300 ATOM 2082 35. 581 52. 026 1. 00 22. 70 OE2 GLU 300 36. 438 -1.319ATOM 2083 2.082 55. 550 1. 00 25. 31 ATOM 2084 C GLU 300 36.734 1. 00 22. 71 1.408 55. 663 ATOM **GLU 300** 37.769 2085 0 5 ATOM 2086 N LEU 301 36.712 3. 409 55. 622 1. 00 26. 47 55. 900 1. 00 26. 65 ATOM 2087 CA LEU 301 37. 919 4. 174 5. 676 55. 992 1. 00 26. 57 LEU 301 37. 600 ATOM 2088 CB1. 00 26. 02 6. 395 54. 701 ATOM 2089 CG LEU 301 37. 165 7. 784 55. 047 1. 00 27. 06 CD1 LEU 301 36.684 ATOM 2090 10 CD2 LEU 301 6. 474 53. 701 1. 00 25. 38 ATOM 2091 38. 312 1. 00 26. 23 3. 648 57. 226 2092 C LEU 301 38. 452 ATOM 3. 209 57. 313 1. 00 26. 97 ATOM 2093 0 LEU 301 39. 594 3.670 58. 259 1. 00 26. 05 VAL 302 37.623 ATOM 2094 N 3. 154 59. 542 1. 00 27. 56 ATOM 2095 CA VAL 302 38.068 15 3. 034 60. 524 1. 00 28. 13 VAL 302 36. 911 ATOM 2096 CB 2. 285 61. 777 1. 00 26. 62 ATOM 2097 CG1 VAL 302 37. 354 4. 424 1.00 30.95 CG2 VAL 302 36. 433 60. 882 ATOM 2098 38.723 1. 786 59. 386 1. 00 27. 42 ATOM 2099 C VAL 302 1. 529 59. 977 1. 00 29. 00 2100 VAL 302 39. 765 20 ATOM 0 0.906 1. 00 25. 04 ATOM 2101 N ARG 303 38. 127 58. 593 -0.3951. 00 25. 12 38.723 58. 417 2102 CA ARG 303 ATOM 37.906 -1.25457. 475 1. 00 26. 51 ATOM 2103 CBARG 303 38. 587 -2.55857. 126 1. 00 28. 11 2104 CG ARG 303 ATOM 1. 00 31. 77 ATOM 2105 CDARG 303 37. 609 -3.52056. 490 25 -4.4561. 00 32. 46 NE ARG 303 38. 260 55. 583 ATOM 2106 **ATOM** 2107 CZARG 303 38. 483 -4.21554. 296 1. 00 34. 64 -3.05953. 759 1. 00 33. 51 ATOM 2108 NH1 ARG 303 38. 103 NH2 ARG 303 39. 082 53. 546 1. 00 35. 80 ATOM 2109 -5. 136

- 217 -ATOM 2110 C 1. 00 27. 77 ARG 303 40. 111 -0. 242 57. 854 ATOM 2111 0 ARG 303 41.073 -0.78858. 401 1. 00 30. 47 2112 N LEU 304 0.495 ATOM 40. 236 56. 754 1. 00 27. 67 LEU 304 0.674 1.00 24.93 ATOM 2113 CA 41. 562 56. 147 CB LEU 304 1.526 1.00 22.51 5 ATOM 2114 41.464 54. 865 0.902 ATOM 2115 CG LEU 304 40.640 53. 718 1. 00 19. 14 ATOM CD1 LEU 304 2116 40.386 1.957 52. 675 1. 00 19. 15 CD2 LEU 304 ATOM 2117 41. 352 -0. 295 53. 105 1. 00 14. 45 LEU 304 ATOM 2118 C 42. 523 1. 290 57. 168 1. 00 21. 35 ATOM 2119 0 LEU 304 43. 584 0.736 57. 432 1. 00 20. 90 10 **ATOM** 2120 N VAL 305 42. 142 2.406 57. 770 1.00 17.52 2121 **ATOM** CA VAL 305 43.003 3. 011 58. 758 1. 00 17. 43 **ATOM** 2122 CBVAL 305 42. 316 4. 162 59. 423 1. 00 14. 40 2123 ATOM CG1 VAL 305 43. 154 4.673 60. 583 1.00 14.53 15 ATOM 2124 CG2 VAL 305 42.095 5. 240 58. 408 1.00 14.33 ATOM 2125 C VAL 305 43. 400 2.010 59. 829 1. 00 20. 92 ATOM 2126 0 VAL 305 44. 497 2.071 60. 387 1. 00 22. 69 2127 N LEU 306 42.502 1.085 ATOM 60. 126 1. 00 24. 02 2128 LEU 306 42. 783 0.081 ATOM CA 61. 144 1. 00 26. 64 ATOM 2129 CB 41. 481 -0.58520 LEU 306 61. 594 1. 00 27. 02 2130 CG -0.56363.087 ATOM LEU 306 41. 154 1. 00 27. 64 2131 41.094 ATOM CD1 LEU 306 0.873 63. 592 1. 00 27. 51 ATOM 2132 CD2 LEU 306 39. 826 -1.26763. 311 1. 00 28. 07 ATOM 2133 C LEU 306 43. 721 -0. 965 60. 566 1. 00 27. 73 2134 25 ATOM 0 LEU 306 44. 745 -1.30361. 157 1. 00 26. 86 **ATOM** 2135 LEU 307 43. 360 -1.467N 59. 394 1. 00 28. 77 ATOM 2136 CA LEU 307 44. 156 -2.47858. 733 1. 00 32. 47 ATOM 2137 CB LEU 307 -2.89343. 465 57. 437 1. 00 29. 90 ATOM 2138 CG LEU 307 43. 477 -4. 392 1. 00 29. 19 57. 130

- 218 -ATOM 2139 CD1 LEU 307 43. 104 -5. 210 58. 361 1. 00 28. 38 ATOM CD2 LEU 307 56. 015 1. 00 29. 88 2140 42. 495 -4. 648 ATOM C LEU 307 45. 553 -1.91658. 466 1. 00 35. 49 2141 ATOM 2142 0 LEU 307 46. 542 -2.64558. 394 1. 00 36. 50 2143 N ARG 308 45.622 -0.602**ATOM** 58. 332 1. 00 38. 03 5 **ATOM** 2144 CA ARG 308 46.882 0.080 58. 101 1. 00 41. 29 CB ARG 308 ATOM 2145 46. 603 1. 580 57. 936 1. 00 47. 88 ATOM 2146 CG ARG 308 47.706 2. 544 58. 368 1.00 54.88 ATOM CD ARG 308 2.693 2147 48. 819 57. 338 1. 00 60. 14 ATOM 2148 NE ARG 308 49. 524 3. 958 57. 540 1.00 65.47 10 ATOM 2149 CZARG 308 50. 523 4. 401 56. 784 1. 00 67. 54 ATOM 2150 NH1 ARG 308 3. 673 50. 954 55. 757 1. 00 68. 57 ATOM 2151 NH2 ARG 308 51.074 5. 584 57. 046 1.00 66.83 **ATOM** 2152 C ARG 308 47. 783 -0.18259.301 1. 00 40. 42 ATOM 2153 0 ARG 308 48. 889 -0.69459. 159 1.00 40.04 15 ATOM 2154 N 47. 287 0. 152 LEU 309 60. 487 1. 00 39. 27 -0.027ATOM 2155 CA LEU 309 48. 043 61. 717 1. 00 38. 92 ATOM 2156 CBLEU 309 47. 224 0.484 62. 895 1. 00 33. 74 ATOM 46.852 2157 CG LEU 309 1. 958 62. 854 1. 00 30. 26 ATOM 2158 CD1 LEU 309 45. 453 2. 121 63. 368 1. 00 30. 84 20 ATOM 2159 CD2 LEU 309 47.819 2. 766 63.683 1. 00 27. 57 ATOM 2160 C LEU 309 48. 461 -1.47361. 984 1. 00 41. 92 ATOM 2161 0 LEU 309 49.600 -1.74162. 364 1. 00 42. 73 ATOM 2162 VAL 310 47. 541 -2.40661. 788 N 1. 00 44. 59 **ATOM** 2163 VAL 310 -3.811CA 47. 829 62. 039 1.00 46.67 25 **ATOM** 2164 CBVAL 310 46.606 -4.65161. 798 1.00 46.95 ATOM 2165 CG1 VAL 310 45. 419 -4.00662. 479 1.00 49.54 CG2 VAL 310 ATOM 2166 46. 368 -4.77960. 312 1. 00 47. 77 1.00 47.55 ATOM 2167 C VAL 310 61. 139 48. 929 **-**4. 321

- 219 -ATOM 2168 0 VAL 310 49. 488 -5. 392 61. 374 1. 00 48. 66 ATOM 2169 N ASP 311 49. 217 -3. 559 60. 093 1. 00 48. 93 ATOM 2170 CA ASP 311 50. 262 -3.92759. 160 1. 00 52. 04 ATOM 2171 CBASP 311 49. 993 -3.29857. 793 1. 00 57. 14 ATOM 2172 CG ASP 311 48.752 -3.8695 57. 135 1.00 61.79 ATOM 2173 OD1 ASP 311 48. 348 -3.37756.054 1. 00 63. 59 OD2 ASP 311 ATOM 2174 48. 180 -4.81957. 713 1. 00 63. 98 ASP 311 ATOM 2175 С 51.618 -3.49059. 698 1. 00 51. 94 ATOM 2176 ASP 311 -4.2560 52. 580 59.653 1. 00 53. 89 10 ATOM 2177 N GLU 312 51. 702 -2. 267 60. 212 1. 00 49. 51 ATOM 2178 52. 961 -1.785CA GLU 312 60. 762 1. 00 47. 68 ATOM 2179 CBGLU 312 53. 071 -0. 272 60. 632 1. 00 48. 44 2180 **ATOM** CG GLU 312 52.900 0. 221 59. 216 1. 00 51. 79 ATOM 2181 CD GLU 312 53. 122 1. 713 59. 084 1. 00 53. 56 2182 0E1 GLU 312 52.698 2. 280 15 ATOM 58. 047 1. 00 49. 90 ATOM 2183 OE2 GLU 312 53. 725 2. 309 60. 013 1. 00 56. 82 ATOM 2184 53.075 -2.172C GLU 312 62. 222 1. 00 46. 11 ATOM 2185 0 GLU 312 53. 514 -1.37763.049 1. 00 46. 75 2186 ATOM N ASN 313 52.666 -3.39762. 527 1. 00 45. 02 20 ATOM 2187 CA ASN 313 52. 720 -3.93863.879 1. 00 44. 64 **ATOM** 2188 CB ASN 313 54. 100 -4.55064. 119 1. 00 43. 84 ATOM 2189 CG ASN 313 54. 028 -5.86064. 863 1. 00 45. 16 ATOM 2190 OD1 ASN 313 53. 377 -5. 965 65. 906 1. 00 43. 79 ATOM 2191 ND2 ASN 313 54. 701 -6. 875 64. 333 1. 00 46. 05 ATOM 2192 C ASN 313 52. 408 -2.92164. 991 25 1. 00 44. 49 ATOM 2193 0 ASN 313 53. 303 -2.50965. 728 1. 00 45. 19 ATOM 2194 N LEU 314 51. 142 -2. 530 65. 126 1. 00 43. 02 ATOM 2195 CA LEU 314 50. 743 -1.56366. 159 1. 00 40. 80 ATOM 2196 CBLEU 314 50. 639 -0. 167 65. 549 1. 00 34. 97

- 220 -ATOM 2197 CG LEU 314 51. 940 0. 499 65. 127 1.00 29.58 **ATOM** CD1 LEU 314 2198 51. 698 1. 453 63. 981 1. 00 28. 94 ATOM 2199 CD2 LEU 314 52. 516 1. 212 66. 311 1. 00 28. 16 ATOM 2200 C LEU 314 49. 396 -1.92466. 777 1. 00 42. 38 2201 0 ATOM LEU 314 49. 026 -1.42267. 848 1.00 39.73 5 ATOM 2202 N LEU 315 48. 689 -2.81266.078 1.00 44.49 2203 ATOM CA LEU 315 47. 352 -3.26866. 439 1. 00 45. 22 ATOM 2204 CB LEU 315 46. 354 -2.69565. 445 1. 00 43. 49 2205 ATOM CG LEU 315 45. 121 66.045 -2.0631. 00 43. 28 ATOM 2206 CD1 LEU 315 44.055 -1.9761.00 43.01 10 64. 972 2207 CD2 LEU 315 ATOM 44. 643 -2.90767. 209 1.00 46.13 ATOM 2208 C LEU 315 47. 214 -4. 781 66. 407 1.00 46.34 **ATOM** 2209 0 47. 828 LEU 315 -5.43965. 577 1.00 47.74 ATOM 2210 N PHE 316 46. 380 -5. 318 67. 292 1.00 48.50 CA 2211 15 ATOM PHE 316 46. 125 -6.76067. 369 1. 00 50. 80 ATOM 2212 CBPHE 316 45. 054 -7. 186 66. 347 1. 00 48. 89 2213 ATOM CG PHE 316 43. 829 -6.31266. 331 1. 00 46. 47 ATOM 2214 CD1 PHE 316 43. 163 -5. 999 67. 508 1. 00 45. 93 CD2 PHE 316 ATOM 2215 43. 350 -5.79165. 134 1. 00 44. 48 20 ATOM 2216 CE1 PHE 316 42. 043 -5. 183 67. 491 1.00 44.57 ATOM 2217 CE2 PHE 316 42. 229 -4. 974 65. 109 1. 00 43. 59 ATOM 2218 CZPHE 316 41. 577 -4. 669 66. 290 1.00 44.05 2219 C ATOM PHE 316 47. 371 -7. 605 67. 124 1. 00 53. 06 2220 ATOM 0 PHE 316 47. 342 -8. 521 66. 299 1.00 54.62 ATOM 2221 HIS 317 25 N 48. 456 -7.30467. 835 1. 00 54. 60 ATOM 2222 CA HIS 317 49.710 -8.04667. 691 1. 00 55. 95 ATOM 2223 CBHIS 317 49. 676 -9.30168. 569 1. 00 54. 90 ATOM 2224 CG HIS 317 49. 708 -9.00470.034 1. 00 55. 21 **ATOM** 2225 CD2 HIS 317 49. 686 -9. 823 71. 113 1. 00 55. 22

- 221 -**ATOM** 2226 ND1 HIS 317 49. 778 -7. 718 70. 528 1. 00 54. 55 49. 798 -7. 756 1. 00 55. 21 ATOM 2227 CE1 HIS 317 71. 848 NE2 HIS 317 49. 744 -9. 020 72. 229 1.00 56.90 ATOM 2228 ATOM 2229 C HIS 317 50. 004 -8. 426 66. 240 1. 00 58. 27 HIS 317 50. 521 -9. 514 65. 950 1. 00 58. 90 ATOM 2230 0 5 **ATOM** 2231 N **GLY 318** 49. 665 -7. 513 65. 335 1.00 59.86 **ATOM** 2232 CA **GLY 318** 49. 881 -7. 734 63. 921 1.00 60.72 2233 C **GLY 318** 49. 290 -9. 022 63. 379 1. 00 62. 25 ATOM 50. 031 -9. 956 1. 00 63. 75 ATOM 2234 0 GLY 318 63. 080 2235 N GLU 319 47. 962 -9. 087 63. 277 1. 00 62. 86 10 ATOM ATOM 2236 GLU 319 47. 277 -10. 257 62.716 1. 00 62. 72 CA 2237 GLU 319 47. 663 -11. 545 63. 439 1. 00 66. 93 ATOM CB 1. 00 73. 23 2238 ATOM CG GLU 319 47. 437 -12. 784 62. 575 2239 CD GLU 319 47. 862 -14. 068 63. 262 1. 00 78. 58 ATOM 2240 49. 020 -14. 129 1. 00 80. 57 15 ATOM 0E1 GLU 319 63. 745 ATOM 2241 0E2 GLU 319 47. 043 -15. 019 63. 310 1. 00 81. 49 ATOM 2242 C GLU 319 45. 765 -10. 097 62. 739 1. 00 59. 42 2243 45. 098 -10. 387 63. 735 1. 00 57. 03 ATOM 0 GLU 319 45. 246 -9. 643 **ATOM** 2244 N ALA 320 61. 604 1. 00 55. 74 43. 828 -9. 394 ATOM 2245 CA ALA 320 61. 414 1. 00 54. 02 20 ATOM 2246 CB ALA 320 43. 657 -8. 357 60. 338 1. 00 52. 55 2247 C ALA 320 43. 052 -10. 650 61. 043 1. 00 54. 49 ATOM 2248 ALA 320 43. 620 -11. 565 60. 457 1. 00 55. 61 ATOM 0 1. 00 55. 01 61. 388 ATOM 2249 N SER 321 41. 762 -10. 698 25 ATOM 2250 CA SER 321 40. 924 -11. 856 61.050 1. 00 55. 90 2251 **ATOM** CBSER 321 39. 649 -11. 911 61. 895 1. 00 56. 08 ATOM 2252 0G SER 321 38. 814 -12. 975 61. 445 1. 00 53. 96 2253 C SER 321 40. 513 -11. 780 59. 589 1. 00 55. 49 ATOM 2254 0 SER 321 40. 367 -10. 689 59. 041 1. 00 54. 92 ATOM

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- 222 -ATOM 2255 N GLU 322 40. 292 -12. 933 58. 967 1. 00 54. 84 2256 **GLU 322** ATOM CA 39. 917 -12. 951 1. 00 56. 14 57. 563 ATOM 2257 CB**GLU 322** 39. 646 -14. 382 57. 092 1. 00 58. 38 ATOM 2258 CG **GLU 322** 40. 173 -14. 697 55. 681 1. 00 63. 26 2259 ATOM CD **GLU 322** 41. 712 -14. 670 55. 574 5 1. 00 66. 36 ATOM 2260 OE1 GLU 322 42. 296 -13. 571 55. 432 1. 00 66. 15 2261 ATOM 0E2 GLU 322 42. 339 -15. 754 55. 637 1. 00 66. 78 2262 ATOM C **GLU 322** 38. 685 -12. 085 57. 354 1. 00 55. 71 2263 ATOM 0 GLU 322 38. 343 -11. 727 56. 227 1. 00 54. 93 ATOM 2264 N GLN 323 38. 027 -11. 740 1. 00 55. 82 10 58. 454 2265 ATOM CA GLN 323 36. 838 -10. 904 58. 393 1. 00 55. 20 2266 CB ATOM GLN 323 35. 995 -11. 101 1. 00 57. 22 59. 659 2267 ATOM CG GLN 323 35. 737 -12. 571 59. 983 1. 00 60. 42 ATOM 2268 CD GLN 323 34. 801 -12. 778 61. 164 1. 00 62. 11 ATOM 2269 OE1 GLN 323 34. 596 -13. 909 61. 612 1. 00 63. 58 15 ATOM 2270 NE2 GLN 323 34. 223 -11. 690 1. 00 61. 37 61. 668 2271 ATOM C GLN 323 37. 259 -9. 445 58. 249 1. 00 53. 59 ATOM 2272 0 GLN 323 36. 963 -8. 800 57. 242 1. 00 53. 27 ATOM 2273 N LEU 324 37. 973 -8.93659. 248 1. 00 50. 98 ATOM 2274 CA LEU 324 38. 430 -7.55320 59. 224 1. 00 48. 40 ATOM 2275 CBLEU 324 39. 396 -7.29460. 378 1. 00 46. 63 ATOM 2276 CG LEU 324 39. 956 -5.87660. 498 1. 00 44. 87 ATOM 2277 CD1 LEU 324 38. 846 -4.83760. 390 1. 00 44. 21 ATOM 2278 CD2 LEU 324 40. 671 -5. 758 61. 827 1. 00 43. 22 ATOM 2279 C LEU 324 39. 115 -7.22425 57. 911 1. 00 47. 25 ATOM 2280 0 LEU 324 -6.06539. 181 57. 505 1. 00 44. 86 ATOM 2281 N ARG 325 39. 627 -8. 253 57. 252 1. 00 48. 35 2282 ATOM CA ARG 325 40. 309 -8.05755. 988 1. 00 50. 22 ATOM 2283

CB

ARG 325

41. 473 -9. 055

55. 839

1. 00 53. 47

- 223 -**ATOM** 2284 CG ARG 325 42. 580 -8. 896 56. 894 1.00 57.97 ATOM 2285 CDARG 325 43. 660 -9. 986 56. 808 1. 00 61. 92 ATOM 2286 NE ARG 325 44. 564 -9. 957 57. 966. 1. 00 67. 95 2287 CZATOM ARG 325 45. 535 -10. 844 58. 206 1. 00 70. 27 5 ATOM 2288 NH1 ARG 325 45. 753 -11. 854 57. 371 1.00 69.69 ATOM 2289 NH2 ARG 325 46. 290 -10. 725 59. 293 1.00 70.39 2290 ATOM C ARG 325 39. 320 -8. 224 54. 850 1.00 48.80 ATOM 2291 0 ARG 325 39. 617 -8. 859 53. 847 1.00 50.46 ATOM 2292 N THR 326 38. 131 -7. 663 54. 999 1.00 46.54 10 ATOM 2293 CA THR 326 37. 162 -7. 783 53. 929 1.00 45.13 ATOM 2294 CBTHR 326 36. 108 -8. 810 54. 264 1.00 44.85 ATOM 2295 OG1 THR 326 36. 749 -10. 061 54. 546 1.00 44.98 **ATOM** 2296 CG2 THR 326 1.00 43.46 35. 160 -8. 973 53. 092 ATOM 2297 C THR 326 36. 500 -6. 453 53. 687 1.00 44.79 ATOM 2298 15 0 THR 326 36. 256 -5. 705 54. 626 1.00 45.01 ATOM 2299 N ARG 327 36. 216 -6. 143 52. 430 1. 00 45. 02 2300 ATOM CA ARG 327 35. 590 -4.86652. 136 1.00 45.97 2301 ATOM CB ARG 327 35. 476 -4.65550. 623 1.00 48.63 ATOM 2302 CG ARG 327 34. 961 **-**3. 283 50. 229 1.00 53.97 20 ATOM 2303 CD ARG 327 34. 975 -3.07248. 722 1.00 58.44 **ATOM** 2304 NE ARG 327 33. 747 -2.41048. 282 1.00 66.14 ATOM 2305 CZ ARG 327 33. 387 -1.17848.648 1.00 69.53 **ATOM** 2306 NH1 ARG 327 34. 167 -0.47149. 458 1.00 69.84 ATOM NH2 ARG 327 2307 32. 242 -0.65248. 220 1. 00 68. 29 ATOM 2308 C ARG 327 25 34. 217 -4.79052. 794 1.00 44.69 ATOM 2309 0 ARG 327 33. 486 -5.78452. 861 1.00 44.55 ATOM 2310 N GLY 328 33. 888 -3.60553. 302 1. 00 42. 14 ATOM 2311 CA GLY 328 32. 606 -3.39453. 952 1.00 37.48 ATOM 2312 С GLY 328 32. 480 -4.00755. 334 1.00 33.00

- 224 -ATOM 2313 0 **GLY 328** 31. 693 -3. 532 56. 148 1. 00 32. 88 -5. 049 55. 601 1. 00 29. 02 ATOM 2314 N ALA 329 33. 258 ALA 329 33. 227 -5.74356. 885 1. 00 26. 22 ATOM 2315 CA 57. 028 CBALA 329 34. 452 -6.6231. 00 28. 65 ATOM 2316 -4.8611. 00 24. 38 ALA 329 33. 092 58. 115 ATOM 2317 C 5 ATOM 2318 0 ALA 329 32. 490 -5.27659. 097 1. 00 26. 43 -3.66358. 091 1. 00 21. 81 ATOM 2319 N PHE 330 33. 663 PHE 330 -2.77659. 242 1. 00 18. 07 ATOM 2320 CA 33. 547 PHE 330 59. 558 1. 00 13. 90 ATOM 2321 CB 34. 887 -2.137CG PHE 330 34. 913 -1.40460.862 1. 00 12. 45 ATOM 2322 10 ATOM 2323 CD1 PHE 330 34. 460 -0.09660. 961 1. 00 12. 64 CD2 PHE 330 61. 995 1. 00 12. 73 ATOM 2324 35. 436 -2.009CE1 PHE 330 1. 00 12. 83 ATOM 2325 34. 535 0. 605 62. 188 ATOM CE2 PHE 330 35. 515 -1.31563. 221 1.00 11.49 2326 ATOM 2327 CZPHE 330 35. 066 -0.00863. 315 1. 00 8. 96 15 PHE 330 32. 528 -1.71658. 886 1. 00 17. 48 ATOM 2328 C 32. 855 -0.70258. 273 1. 00 17. 97 ATOM 2329 0 PHE 330 ATOM N GLU 331 31. 288 -1.97659. 275 1. 00 16. 36 2330ATOM 2331 CA GLU 331 30. 149 -1. 105 58. 998 1. 00 18. 14 28. 865 -1.88959. 308 1. 00 22. 08 ATOM 2332 CBGLU 331 20 28. 790 -3.22658. 546 1. 00 26. 82 ATOM 2333 CG GLU 331 2334 CD GLU 331 28. 183 -4. 382 59. 346 1. 00 28. 86 **ATOM ATOM** 2335 OE1 GLU 331 28. 381 -5. 552 58. 931 1. 00 28. 12 0E2 GLU 331 27. 509 -4.12960.371 1. 00 30. 16 ATOM 2336 59.719 1. 00 16. 36 ATOM 2337 C GLU 331 30. 126 0. 248 25 GLU 331 30. 596 0. 380 60.849 1. 00 16. 97 **ATOM** 2338 0 2339 N THR 332 29. 583 1. 263 59.060 1. 00 14. 04 ATOM 2. 568 59. 695 1. 00 14. 47 ATOM 2340CA THR 332 29. 494 28. 747 58. 825 1. 00 10. 93 ATOM 2341 CB THR 332 3. 562

- 225 -**ATOM** 2342 OG1 THR 332 29. 473 3. 751 57. 611 1. 00 6. 57 4.890 59. 550 1. 00 6. 34 CG2 THR 332 28. 597 ATOM 2343 2. 382 60. 994 1. 00 18. 42 THR 332 28. 725 ATOM 2344 C 2.872 62. 052 1. 00 17. 70 ATOM 2345 0 THR 332 29. 125 1. 00 21. 79 1.671 60. 892 ARG 333 27.609 ATOM 2346 N 5 ATOM ARG 333 26. 783 1. 346 62. 040 1. 00 24. 44 2347 CA 0.001 1. 00 28. 62 ATOM 2348 CB ARG 333 26. 095 61. 764 25. 291 -0.59062. 910 1. 00 34. 65 ATOM CG ARG 333 2349 62. 401 1. 00 39. 87 ARG 333 24. 308 -1.664ATOM 2350 CD ARG 333 24. 953 -2.88761.910 1. 00 43. 42 **ATOM** 2351 NE 10 **ATOM** 2352 CZARG 333 25. 198 -3.96962. 653 1. 00 46. 01 -3.99263. 940 1. 00 45. 10 2353 NH1 ARG 333 24. 852 ATOM -5.0301. 00 43. 75 NH2 ARG 333 25. 791 62. 104 ATOM 2354 27. 638 1. 271 63. 323 1. 00 24. 88 **ATOM** 2355 C ARG 333 2356 ARG 333 27. 242 1. 803 64. 358 1. 00 24. 00 15 ATOM 0 28. 818 0.635 63. 232 1. 00 23. 97 PHE 334 ATOM 2357 N 0.458 1. 00 19. 64 2358 PHE 334 29. 740 64. 371 ATOM CA PHE 334 30. 877 -0.50964. 033 1. 00 20. 52 ATOM 2359 CB 1. 00 24. 74 ATOM 2360 CG PHE 334 30. 420 -1.81363. 468 CD1 PHE 334 29. 469 -2.57464. 121 1. 00 25. 94 ATOM 2361 20 CD2 PHE 334 30. 938 -2.27962. 262 1. 00 26. 47 **ATOM** 2362 2363 CE1 PHE 334 29. 039 -3.78063. 575 1. 00 28. 43 ATOM ATOM 2364 CE2 PHE 334 30. 514 -3. 483 61. 711 1. 00 24. 74 PHE 334 29. 565 **-4**. 233 62. 365 1. 00 26. 41 ATOM 2365 CZPHE 334 30.382 1. 739 1. 00 16. 52 2366 C 64. 842 25 ATOM PHE 334 30. 434 2.020 66.039 1. 00 16. 16 2367 0 ATOM 2368 VAL 335 30. 907 2. 509 63. 905 1. 00 13. 20 ATOM N 1. 00 11. 36 2369 VAL 335 31. 546 3. 752 64. 284 ATOM CA 31. 877 63. 033 1. 00 8. 08 ATOM 2370 CB VAL 335 4. 565

- 226 -ATOM 2371 CG1 VAL 335 32. 113 6.003 63. 402 1.00 8.71 ATOM CG2 VAL 335 33.082 3. 979 62. 358 1. 00 1. 00 2372 **ATOM** VAL 335 30.653 4. 558 65. 249 1. 00 13. 02 2373 C **ATOM** 2374 0 VAL 335 31. 126 5.066 66. 264 1. 00 10. 40 4.640 **ATOM** 2375 N SER 336 29.359 64. 934 1. 00 16. 23 5 ATOM 2376 CA SER 336 28.365 5. 372 65. 740 1. 00 18. 55 ATOM 2377 CB SER 336 27. 017 5. 350 65. 039 1. 00 19. 92 SER 336 26.611 3.999 64. 866 1. 00 25. 40 ATOM 2378 0G **ATOM** 2379 C SER 336 28. 162 4. 766 67. 118 1. 00 17. 99 **ATOM** 2380 0 **SER 336** 27.896 5.465 68. 100 1.00 14.64 10 **ATOM** 2381 N GLN 337 28. 239 3. 445 67. 159 1.00 19.48 ATOM 2382 CA GLN 337 28.061 2. 719 68. 394 1. 00 21. 39 2383 27.995 1. 223 ATOM CB GLN 337 68. 123 1. 00 21. 42 0.800 ATOM 2384 CG GLN 337 26. 829 67. 264 1. 00 23. 07 ATOM 2385 CD GLN 337 26.920 -0.65466. 895 1.00 24.96 15 2386 0E1 GLN 337 27. 243 -1.49667. 735 1. 00 28. 83 ATOM NE2 GLN 337 26. 633 -0.966ATOM 2387 65. 638 1. 00 24. 29 29.260 3.011 **ATOM** 2388 C GLN 337 69. 240 1. 00 20. 91 ATOM 2389 0 GLN 337 29. 205 2.963 70.464 1. 00 23. 32 ATOM 2390 N VAL 338 30. 362 3. 317 68. 584 1. 00 20. 52 20 **ATOM** 2391 CA VAL 338 31. 559 3. 589 1. 00 21. 67 69. 337 2392 CB 32.812 3.470 ATOM VAL 338 68. 443 1. 00 20. 93 ATOM 2393 CG1 VAL 338 34.065 3.624 69. 279 1. 00 19. 79 ATOM 2394 CG2 VAL 338 32. 811 2. 126 67. 739 1. 00 16. 69 25 ATOM 2395 C VAL 338 31. 480 4. 973 69. 977 1. 00 23. 61 ATOM 2396 0 VAL 338 31.385 5.079 71. 203 1. 00 21. 96 2397 N GLU 339 ATOM 31.486 6.020 69. 146 1. 00 25. 05 ATOM 2398 GLU 339 31. 455 7. 406 69. 620 1. 00 26. 21 CA ATOM 2399 CB GLU 339 31. 460 68. 440 1. 00 26. 37 8. 402

- 227 -30. 515 8. 082 67. 282 1. 00 31. 63 ATOM 2400 CG GLU 339 66. 311 GLU 339 9. 267 1.00 36.86 ATOM CD30. 287 2401 ATOM 2402 0E1 GLU 339 29. 542 10. 219 66. 663 1. 00 37. 19 9. 243 65. 187 1.00 37.90 0E2 GLU 339 30.850 ATOM 2403 2404 C GLU 339 30. 299 7. 735 70. 541 1.00 26.44 **ATOM** 5 GLU 339 8. 613 71. 396 1. 00 27. 55 ATOM 2405 0 30. 423 7.017 70.380 1.00 26.30 ATOM SER 340 29. 189 2406 N 7. 246 71. 181 1. 00 25. 08 ATOM 2407 CA SER 340 27. 987 26.861 6. 322 70. 717 1. 00 23. 68 **ATOM** 2408 CB SER 340 ATOM 2409 0G SER 340 27. 191 4.970 70.957 1. 00 23. 58 10 7.065 72.676 1. 00 26. 02 ATOM 2410 C SER 340 28. 211 2411 0 SER 340 27. 415 7. 539 73. 488 1. 00 26. 83 ATOM 6.380 1.00 27.41 2412 N ASP 341 29. 294 73. 033 ATOM **ATOM** 2413 CA ASP 341 29.630 6. 143 74. 434 1. 00 27. 85 ASP 341 28. 939 4. 885 74. 953 1. 00 27. 41 ATOM 2414 CB15 ATOM 2415 CG ASP 341 29. 253 4. 621 76. 410 1. 00 26. 49 1. 00 26. 07 OD1 ASP 341 29.628 5. 591 77. 107 ATOM 2416 ATOM 2417 OD2 ASP 341 29. 117 3.463 76.862 1. 00 25. 64 6.008 ASP 341 31. 128 74. 672 1. 00 28. 59 ATOM 2418 C ATOM 2419 0 ASP 341 31. 757 5. 049 74. 229 1. 00 30. 06 20 THR 342 31.688 6.965 75. 398 1. 00 27. 34 ATOM 2420 N **ATOM** 2421 CATHR 342 33. 105 6. 953 75. 694 1. 00 26. 74 THR 342 33. 681 8. 348 75. 553 1. 00 26. 75 ATOM 2422 CB ATOM 2423 OG1 THR 342 33. 072 9. 217 76. 511 1. 00 25. 10 ATOM 2424 CG2 THR 342 33. 387 8. 881 74. 171 1. 00 29. 29 25 ATOM 2425 C THR 342 33. 292 6. 477 77. 114 1. 00 27. 84 1. 00 27. 29 ATOM 2426 0 THR 342 34. 365 6. 625 77. 692 GLY 343 32. 223 5. 908 77. 662 1. 00 30. 32 ATOM 2427 N CA GLY 343 32. 234 5. 398 79. 020 1. 00 31. 31 ATOM 2428

- 228 -2429 C 32. 970 4.083 79. 178 1. 00 32. 13 ATOM **GLY 343 ATOM** 2430 0 **GLY 343** 33. 765 3. 944 80. 105 1.00 34.00 ATOM ASP 344 32. 712 3. 114 78. 304 1.00 31.93 2431 N ATOM ASP 344 33. 400 1.836 78. 411 1. 00 34. 25 2432 CA 0.857 CBASP 344 32. 592 79. 267 1. 00 38. 13 5 ATOM 2433 0.646 78. 744 1. 00 43. 49 ATOM 2434 CG ASP 344 31. 205 ATOM OD1 ASP 344 30. 399 -0.02979.426 1. 00 47. 59 2435 OD2 ASP 344 1. 159 1. 00 46. 67 ATOM 2436 30. 923 77. 643 **ATOM** 2437 C ASP 344 33. 744 1. 196 77. 075 1. 00 33. 85 1.681 1. 00 32. 12 ATOM 2438 0 ASP 344 33. 354 76. 015 10 0.098 **ATOM** 2439 N ARG 345 34. 490 77. 148 1.00 34.54 -0.6261.00 35.60 ATOM 2440 CA ARG 345 34. 935 75. 968 **ATOM** 2441 CB ARG 345 36. 297 -1.27876. 233 1. 00 35. 33 2442 ARG 345 -0.37076.864 1. 00 35. 88 ATOM CG 37. 339 -1.00615 ATOM 2443 CDARG 345 38. 729 76.879 1. 00 35. 19 ATOM NE ARG 345 39. 507 -0.59778. 054 1. 00 36. 95 2444 ATOM 2445 CZARG 345 39. 984 0.629 78. 275 1. 00 36. 97 NH1 ARG 345 39. 780 1.605 1.00 36.40 ATOM 2446 77. 396 0.885 ATOM 2447 NH2 ARG 345 40.654 79. 394 1. 00 36. 46 -1.716ATOM 2448 C ARG 345 33. 961 75. 551 1. 00 36. 31 20 -2.280ATOM 24490 ARG 345 34. 080 74. 461 1.00 37.64 -2.0202450 LYS 346 33. 004 76. 420 1.00 35.01 ATOM N 2451 CA LYS 346 32. 050 -3.08176. 134 1. 00 33. 81 ATOM 30. 824 -2.97577. 041 1. 00 33. 64 ATOM 2452 CB LYS 346 25 ATOM 2453 CG LYS 346 29. 942 -4.22376. 985 1. 00 33. 85 LYS 346 30. 759 -5. 505 77. 186 **ATOM** 2454 CD 1. 00 31. 48 **ATOM** 2455 CE LYS 346 30.061 -6.69976. 542 1. 00 32. 39 LYS 346 -7.96876. 542 1. 00 30. 01 ATOM 2456 NZ 30. 855 31. 613 -3. 093 . 74. 684 ATOM 2457 C LYS 346 1. 00 33. 18

- 229 -**ATOM** LYS 346 31. 746 -4. 101 73. 995 1.00 31.98 2458 0 1. 00 33. 36 ATOM 2459 N GLN 347 31. 101 -1. 967 74. 214 GLN 347 30. 662 -1.88772. 839 1. 00 34. 32 ATOM 2460 CA **GLN 347** -0.53072. 589 1. 00 37. 17 ATOM 2461 CB 30. 014 -0.57872. 703 1. 00 39. 97 2462 CG GLN 347 28. 510 5 ATOM 27. 905 -1.43671.611 1. 00 43. 97 ATOM 2463 CD GLN 347 ATOM 0E1 GLN 347 28. 219 -2.62671. 491 1. 00 43. 88 2464 -0.83570. 799 1. 00 46. 46 **ATOM** 2465 NE2 GLN 347 27. 039 ATOM 2466 C GLN 347 31. 799 -2.14471.844 1. 00 34. 27 -2.922GLN 347 70. 902 1. 00 35. 29 **ATOM** 2467 0 31. 630 10 ILE 348 -1.50272. 054 1. 00 31. 49 ATOM 2468 N 32. 952 34. 109 -1.67971. 165 1. 00 25. 43 ATOM 2469 CA ILE 348 -0.82671.614 ATOM 2470 CB ILE 348 35. 309 1. 00 21. 01 -0.826CG2 ILE 348 36.369 70. 540 1. 00 15. 50 ATOM 2471 0.606 1. 00 22. 27 **ATOM** 2472 CG1 ILE 348 34. 852 71. 875 15 72. 462 ATOM 2473 CD1 ILE 348 35. 914 1. 509 1. 00 24. 55 -3.139ATOM 2474 C ILE 348 34. 524 71. 211 1. 00 24. 70 -3.7632475 0 ILE 348 34. 793 70. 182 1. 00 23. 36 ATOM 2476 TYR 349 34. 560 -3. 681 72. 421 1. 00 23. 30 ATOM N TYR 349 34. 933 -5.06172. 597 1. 00 23. 65 ATOM 2477 CA 20 2478 TYR 349 34. 727 -5.49174. 047 1. 00 25. 21 ATOM CB TYR 349 34. 779 -6.98974. 221 1. 00 31. 27 **ATOM** 2479 CG 1. 00 33. 98 ATOM 2480 CD1 TYR 349 35. 990 -7.66574. 333 2481 CE1 TYR 349 36. 028 -9.06274. 435 1. 00 36. 98 ATOM 2482 CD2 TYR 349 33. 607 -7. 740 74. 216 1. 00 34. 38 25 ATOM 2483 CE2 TYR 349 33. 628 -9.12574. 312 1.00 36.69 ATOM 2484 TYR 349 34. 837 -9. 786 74. 421 1. 00 37. 89 ATOM CZ TYR 349 34. 834 -11. 165 74. 512 ATOM 2485 0H1. 00 37. 12 ATOM 2486 C TYR 349 34. 105 -5. 945 71. 676 1. 00 23. 47

- 230 -ATOM 2487 0 TYR 349 34. 654 -6. 602 70. 794 1. 00 21. 02 2488 ATOM ASN 350 N 32. 783 -5. 934 71. 872 1. 00 25. 29 **ATOM** 2489 CA ASN 350 31.850 -6.76671. 091 1. 00 25. 07 ATOM 2490 CB ASN 350 30. 379 -6.50071. 482 1. 00 23. 90 5 ATOM 2491 CG ASN 350 30.069 -6.8441.00 25.09 72. 941 **ATOM** 2492 OD1 ASN 350 -7.92430. 413 73. 440 1. 00 22. 84 ATOM 2493 ND2 ASN 350 29.398 -5.9231.00 25.65 73. 626 2494 C ATOM ASN 350 31. 982 -6.62069. 580 1. 00 25. 25 ATOM 2495 ASN 350 0 31. 994 -7.6191. 00 25. 84 68. 859 2496 10 ATOM N ILE 351 32. 068 -5.39269. 083 1. 00 25. 43 ATOM 2497 ILE 351 -5.22767. 642 CA 32. 195 1. 00 25. 64 ATOM 2498 ILE 351 32. 388 CB -3.74567. 248 1. 00 24. 60 2499 ATOM CG2 ILE 351 32. 282 -3.60065. 743 1. 00 23. 69 ATOM 2500 CG1 ILE 351 31. 305 -2.88267. 903 1. 00 22. 24 2501 15 ATOM CD1 ILE 351 31. 357 -1.43167. 509 1. 00 19. 88 ATOM 2502 C ILE 351 33. 415 -6.04767. 224 1. 00 26. 73 ATOM 2503 0 ILE 351 33. 282 -7.04766. 517 1. 00 25. 71 ATOM 2504 N LEU 352 34. 592 -5.62967. 695 1. 00 27. 08 ATOM 2505 CA LEU 352 35. 847 -6.31267. 397 1. 00 27. 36 **ATOM** 20 2506 CBLEU 352 36. 994 -5. 700 68. 206 1. 00 24. 45 ATOM 2507 CG LEU 352 37. 295 -4.20868. 090 1. 00 23. 84 ATOM 2508 CD1 LEU 352 38. 464 -3.83868. 995 1. 00 21. 54 ATOM CD2 LEU 352 2509 37. 620 -3.87266. 660 1. 00 23. 96 ATOM 2510 C LEU 352 35. 746 -7.79867. 737 1. 00 29. 42 2511 0 25 **ATOM** LEU 352 36. 045 -8.67066. 912 1. 00 29. 43 ATOM 2512 N SER 353 35. 336 -8. 087 68. 965 1.00 30.73 ATOM 2513 CA SER 353 35. 206 -9. 468 69. 398 1. 00 32. 72 ATOM CB 2514 SER 353 34. 408 -9. 531 70. 711 1. 00 32. 86 ATOM 2515 0G SER 353 34. 187 -10. 870 71. 126 1. 00 35. 10

- 231 -1. 00 33. 76 ATOM 2516 C SER 353 34. 513 -10. 277 68. 295 67.670 1. 00 34. 42 ATOM 2517 0 SER 353 35. 123 -11. 149 68. 035 1. 00 34. 17 **ATOM** 2518 N THR 354 33. 252 -9. 941 THR 354 32. 437 -10. 621 67. 031 1. 00 32. 96 ATOM 2519 CA ATOM CBTHR 354 30. 999 -10. 073 67.076 1. 00 33. 01 2520 5 1. 00 32. 52 ATOM 2521 OG1 THR 354 30. 120 -10. 980 66. 408 CG2 THR 354 1.00 34.65 ATOM 2522 30. 922 -8. 702 66. 411 ATOM 2523 C THR 354 33. 007 -10. 503 65. 608 1. 00 32. 28 ATOM 2524 0 THR 354 32. 444 -11. 038 64. 646 1. 00 30. 58 **ATOM** 2525 LEU 355 -9.80765. 497 1. 00 31. 47 N 34. 137 10 ATOM 2526 CA LEU 355 34. 832 -9.61264. 227 1. 00 30. 67 1. 00 28. 42 ATOM 2527 CBLEU 355 35. 488 -8.23964. 187 ATOM CG LEU 355 34. 780 -7.24063. 293 1. 00 27. 13 2528 CD1 LEU 355 -5. 874 63. 487 1. 00 26. 09 ATOM 2529 35. 387 ATOM 2530 CD2 LEU 355 34. 898 -7.69861.859 1. 00 27. 39 15 1. 00 31. 14 ATOM 2531 C LEU 355 35. 905 -10. 668 64.061 ATOM 2532 0 LEU 355 36. 573 -10. 735 63. 033 1. 00 30. 59 2533 N GLY 356 36. 074 -11. 484 65.091 1.00 32.64 ATOM **ATOM** 2534 CA GLY 356 37. 068 -12. 530 65. 030 1.00 35.49 ATOM 2535 C GLY 356 38. 435 -12. 074 65. 493 1. 00 37. 44 20 ATOM 2536 0 GLY 356 39. 443 -12. 492 64. 930 1. 00 37. 31 2537 N LEU 357 38. 471 -11. 222 66. 516 1.00 39.40 ATOM ATOM 2538 CA LEU 357 39. 729 -10. 717 67.057 1. 00 41. 85 ATOM 2539 CB LEU 357 39. 898 -9. 239 66. 705 1. 00 41. 35 CG LEU 357 39. 816 -8. 876 65. 218 1. 00 43. 17 25 ATOM 2540 ATOM 2541 CD1 LEU 357 39. 953 -7. 375 65.064 1. 00 42. 98 CD2 LEU 357 40. 904 -9. 585 1. 00 43. 93 ATOM 2542 64. 428 39. 759 -10. 888 68. 571 1. 00 44. 59 ATOM 2543 C LEU 357

ATOM

2544 0

LEU 357

38. 750 -11. 247

69. 176

1. 00 45. 94

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	ATOM	2545	N	ARG	358	40. 919	-10. 643	69. 178	1. 00 46. 55
	ATOM	2546	CA	ARG	358	41. 080	-10. 752	70. 632	1. 00 48. 12
	ATOM	2547	CB	ARG	358	42. 113	-11. 819	70. 994	1. 00 52. 19
	ATOM	2548	CG	ARG	358	41. 649	-13. 258	70. 839	1. 00 61. 21
5	ATOM	2549	CD	ARG	358	40. 870	-13. 768	72. 064	1. 00 68. 48
	ATOM	2550	NE	ARG	358	39. 519	-13. 206	72. 184	1. 00 74. 00
	ATOM	2551	CZ	ARG	358	38. 629	-13. 577	73. 104	1. 00 75. 57
	ATOM	2552	NH1	ARG	358	38. 935	-14. 517	73. 998	1. 00 75. 58
	ATOM	2553	NH2	ARG	358	37. 431	-13. 005	73. 131	1. 00 74. 54
10	ATOM	2554	C	ARG	358	41. 558	-9. 418	71. 174	1. 00 46. 76
	ATOM	2555	0	ARG	358	42. 702	-9. 284	71. 580	1. 00 49. 52
	ATOM	2556	N	PRO	359	40. 679	-8. 412	71. 197	1. 00 45. 33
	ATOM	2557	CD	PRO	359	39. 271	-8. 532	70. 791	1. 00 45. 90
	ATOM	2558	CA	PRO	359	40. 956	-7. 056	71. 677	1. 00 44. 06
15	ATOM	2559	CB	PRO	359	39. 565	-6. 449	71. 784	1. 00 45. 14
	ATOM	2560	CG	PR0	359	38. 865	-7. 086	70. 643	1. 00 46. 70
	ATOM	2561	C	PR0	359	41. 725	-6. 936	72. 986	1. 00 42. 11
	ATOM	2562	0	PR0	359	41. 662	-7. 797	73. 860	1. 00 42. 98
	ATOM	2563	N	SER	360	42. 449	-5. 840	73. 118	1. 00 38. 55
20	ATOM	2564	CA	SER	360	43. 209	-5. 608	74. 321	1. 00 35. 42
	ATOM	2565	CB	SER	360	44. 701	-5. 624	74. 014	1. 00 38. 45
	ATOM	2566	0G	SER	360	45. 100	-4. 379	73. 453	1. 00 37. 32
	ATOM	2567	C	SER	360	42. 847	-4. 234	74. 818	1. 00 33. 26
	ATOM	2568	0	SER	360	42. 530	-3. 345	74. 028	1. 00 30. 55
25	ATOM	2569	N	THR	361	42. 907	-4. 060	76. 128	1. 00 31. 87
	ATOM	2570	CA	THR	361	42. 625	-2.771	76. 721	1. 00 33. 02
	ATOM	2571	CB	THR	361	43. 285	-2. 646	78. 083	1. 00 32. 00
	ATOM	2572	0G1	THR	361	42. 697	-3. 593	78. 981	1. 00 31. 30
	ATOM	2573	CG2	THR	361	43. 135	-1. 223	78. 618	1. 00 28. 90

- 233 -2574 C ATOM THR 361 43. 162 -1. 637 75. 853 1. 00 35. 59 ATOM 2575 THR 361 0 42. 600 -0. 545 75. 837 1. 00 37. 16 2576 **ATOM** N THR 362 44. 253 -1.87975. 135 1. 00 37. 62 **ATOM** 2577 THR 362 44. 812 CA -0.81974. 303 1. 00 37. 63 5 ATOM 2578 CB THR 362 46. 341 -0.94974. 156 1.00 38.04 2579 OG1 THR 362 ATOM 46. 950 -0.98175. 453 1. 00 37. 77 2580 CG2 THR 362 46.890 ATOM 0. 242 73. 395 1.00 37.49 2581 C ATOM THR 362 44. 183 -0.83972. 928 1.00 36.67 ATOM 2582 0 THR 362 0. 194 43. 758 72. 416 1.00 34.48 ATOM 2583 10 N ASP 363 44. 132 -2.03272. 345 1. 00 37. 88 ATOM 2584 CA ASP 363 43. 555 -2.24671. 024 1. 00 40. 18 ATOM 2585 CBASP 363 43. 238 -3.72970. 842 1. 00 42. 13 2586 ATOM CG ASP 363 44. 477 -4.55770.666 1. 00 45. 73 ATOM 2587 OD1 ASP 363 44. 433 -5. 779 70. 932 1.00 49.54 ATOM 2588 OD2 ASP 363 45. 500 15 -3.97670. 247 1.00 46.04 **ATOM** 2589 C ASP 363 42. 289 -1.42970. 841 1. 00 40. 28 2590 ASP 363 ATOM 0 42.070 -0.80169. 802 1. 00 38. 03 2591 ATOM N CYS 364 41. 455 -1.44971.871 1. 00 41. 60 **ATOM** 2592 CA CYS 364 40. 197 -0.72471. 849 1. 00 41. 33 ATOM 2593 CBCYS 364 20 39. 426 -1.03673. 131 1. 00 41. 81 **ATOM** 2594 SG. CYS 364 39. 078 -2.81873. 225 1. 00 41. 98 ATOM 2595 C CYS 364 40. 447 0.766 71.685 1. 00 39. 78 ATOM 2596 CYS 364 1.00 37.44 0 39. 991 1. 382 70. 721 2597 ATOM N ASP 365 41. 194 1. 333 72. 622 1. 00 38. 65 **ATOM** 2598 ASP 365 41. 525 25 CA 2. 744 72. 580 1. 00 37. 87 ATOM 2599 CBASP 365 42. 498 3.060 73.709 1.00 39.53 ATOM 2600 CG ASP 365 42.073 2. 424 75. 014 1. 00 42. 28 ATOM 2601 OD1 ASP 365 40. 887 2. 000 75. 096 1.00 43.06 OD2 ASP 365 ATOM 2602 42. 908 2. 355 75. 949 1.00 41.82

- 234 -ATOM 2603 C ASP 365 42. 123 3. 092 71. 220 1. 00 35. 70 **ATOM** 2604 0 ASP 365 41.887 4. 173 70.682 1. 00 35. 49 ATOM 2605 N ILE 366 42. 895 2. 175 70.655 1. 00 32. 72 **ATOM** 2606 CA ILE 366 2.428 43. 469 69. 347 1. 00 31. 21 ATOM 2607 CB ILE 366 44. 345 1. 241 68.891 1.00 30.98 5 ATOM CG2 ILE 366 2608 44. 878 1. 488 67. 482 1. 00 30. 08 ATOM 2609 CG1 ILE 366 1.010 45. 472 69. 907 1. 00 30. 05 ATOM CD1 ILE 366 2610 46. 426 2. 165 70.071 1. 00 26. 19 **ATOM** 2611 C ILE 366 42. 292 2.622 68. 384 1. 00 30. 65 10 ATOM 2612 0 ILE 366 42. 140 3.686 67.790 1. 00 29. 65 **ATOM** 2613 N VAL 367 41. 451 1. 598 68. 255 1. 00 29. 81 **ATOM** 2614 CA VAL 367 40. 287 1.665 67. 378 1. 00 27. 24 **ATOM** 2615 CB VAL 367 39. 397 0.424 67. 541 1. 00 26. 77 ATOM 2616 CG1 VAL 367 38. 193 0.520 66.630 1. 00 25. 16 ATOM 2617 CG2 VAL 367 -0.81715 40. 190 67. 220 1. 00 27. 90 ATOM 2618 C VAL 367 39. 453 2. 910 67. 657 1. 00 26. 82 ATOM 2619 0 VAL 367 39.061 3.606 1. 00 27. 16 66. 727 **ATOM** 2620 N ARG 368 39. 171 3. 191 68. 927 1. 00 25. 49 ATOM 2621 CA ARG 368 38. 398 4. 380 69. 266 1. 00 24. 26 **ATOM** 2622 20 CB ARG 368 38. 431 4. 644 70. 772 1. 00 23. 73 ATOM 2623 CG ARG 368 37. 765 5. 951 71. 217 1. 00 26. 32 ATOM 2624 CD ARG 368 36. 239 5. 948 71.033 1. 00 32. 00 ATOM 2625 NE ARG 368 35. 542 5. 015 71. 926 1. 00 33. 36 ATOM 2626 CZARG 368 35. 558 5.096 73. 253 1. 00 33. 30 **ATOM** 2627 NH1 ARG 368 25 36. 237 6.069 73. 843 1. 00 36. 87 ATOM 2628 NH2 ARG 368 34.904 4. 209 73. 990 1. 00 30. 08 ATOM 2629 C ARG 368 39. 034 5. 545 68. 539 1. 00 25. 24 ATOM 2630 0 ARG 368 38. 403 6. 175 67.700 1. 00 26. 08 **ATOM** 2631 N ARG 369 40. 299 5.808 68. 844 1. 00 26. 69

- 235 -**ATOM** 2632 ARG 369 CA 41. 022 6. 905 68. 226 1. 00 28. 80 ATOM 2633 CB ARG 369 42. 500 6. 842 68. 619 1. 00 33. 81 ATOM 2634 ARG 369 CG 42. 992 8. 041 69. 421 1. 00 41. 54 2635 ATOM CD ARG 369 44. 246 8. 666 68. 797 1. 00 47. 78 5 ATOM 2636 NE ARG 369 44. 827 9. 709 69. 642 1. 00 53. 83 2637 ATOM CZARG 369 45. 436 9. 479 70.803 1. 00 57. 34 ATOM 2638 NH1 ARG 369 45. 547 8. 234 71. 256 1. 00 57. 39 **ATOM** 2639 NH2 ARG 369 45. 925 10. 492 71. 517 1. 00 58. 51 ATOM 2640 C ARG 369 40.888 6. 941 66. 704 1. 00 27. 66 10 ATOM 2641 0 ARG 369 40.898 8.017 66. 116 1. 00 27. 35 ATOM 2642 N ALA 370 40.760 5. 778 66.071 1. 00 28. 23 2643 ATOM CA ALA 370 40.622 5. 699 64. 613 1. 00 29. 69 2644 ATOM CBALA 370 40.779 4. 264 64. 144 1. 00 27. 18 ATOM 2645 C ALA 370 39. 266 6.218 64. 184 1. 00 32. 49 ATOM 2646 0 15 ALA 370 39. 155 7.084 63. 313 1. 00 33. 37 ATOM 2647 N CYS 371 38. 229 5. 663 64. 797 1. 00 35. 80 **ATOM** 2648 CA CYS 371 36.860 6.053 64. 500 1. 00 37. 09 ATOM 2649 CB CYS 371 35. 892 5. 310 65. 427 1. 00 37. 67 ATOM 2650 SG CYS 371 35.709 3. 539 65. 052 1. 00 43. 56 **ATOM** 20 2651 C ·CYS 371 36. 692 7. 555 64. 663 1. 00 36. 66 **ATOM** 2652 0 CYS 371 36. 237 8. 231 63. 746 1. 00 36. 14 ATOM 2653 N GLU 372 37. 079 8.065 65. 829 1. 00 36. 70 ATOM 2654 GLU 372 CA 36. 962 9. 482 66. 140 1. 00 37. 83 ATOM 2655 GLU 372 CB 37. 440 9.741 67. 569 1. 00 41. 72 25 **ATOM** 2656 CG GLU 372 37.405 11. 202 67. 993 1. 00 50. 44 ATOM 2657 CD GLU 372 38.615 11. 981 67. 504 1. 00 56. 78 ATOM 2658 0E1 GLU 372 39. 747 11.656 67. 940 1. 00 60. 05 ATOM 0E2 GLU 372 2659 38. 437 12. 914 66. 685 1. 00 59. 31 ATOM 2660 C GLU 372 37. 736 10. 344 65. 163 1. 00 36. 14

- 236 -ATOM 2661 0 GLU 372 37. 280 11. 410 64. 745 1. 00 34. 24 ATOM 2662 SER 373 38. 917 9.890 64. 793 N 1. 00 37. 31 ATOM 2663 SER 373 39. 703 10.662 63.856 CA 1. 00 39. 48 ATOM 2664 CB SER 373 41.095 10.040 63.694 1.00 40.54 **ATOM** 2665 0G **SER 373** 41.014 8.697 63. 253 1.00 41.31 5 ATOM 2666 C **SER 373** 38. 966 10.713 62. 516 1.00 38.54 ATOM 2667 0 SER 373 38. 778 11. 790 61.953 1.00 39.30 38. 528 ATOM 2668 N VAL 374 9. 552 62.029 1. 00 35. 74 ATOM 2669 VAL 374 37. 817 9.462 1.00 34.53 CA 60. 755 **ATOM** 7. 987 2670 CB VAL 374 37. 519 60.388 1. 00 33. 30 10 ATOM 2671 CG1 VAL 374 36.688 7.897 59. 119 1.00 30.40 ATOM 2672 CG2 VAL 374 38. 811 7. 257 1. 00 34. 78 60. 186 2673 C 36. 512 10. 250 ATOM VAL 374 60. 736 1. 00 35. 17 2674 0 ATOM VAL 374 36. 253 11.010 59. 797 1.00 34.51 ATOM 2675 N SER 375 35. 700 10.080 15 61. 775 1. 00 35. 24 ATOM 2676 CA SER 375 34. 416 10. 768 61.866 1. 00 34. 91 2677 CB 33.641 ATOM SER 375 10. 312 63. 103 1. 00 35. 91 2678 33. 802 **ATOM** 0GSER 375 11. 230 64. 178 1. 00 37. 28 ATOM 2679 C SER 375 34. 585 12. 272 61. 933 1. 00 34. 67 2680 33.865 ATOM 0 SER 375 13. 010 61. 266 1. 00 35. 17 20 2681 ATOM N THR 376 35. 534 12.725 62. 743 1. 00 34. 00 **ATOM** 2682 CA THR 376 35. 768 14. 150 62.889 1. 00 35. 55 ATOM 2683 CB THR 376 36. 827 14. 421 63.954 1. 00 38. 06 ATOM 2684 OG1 THR 376 36. 461 13. 739 65. 158 1. 00 40. 51 **ATOM** 2685 CG2 THR 376 36.926 15. 923 25 64. 239 1. 00 38. 22 2686 **ATOM** C THR 376 36. 208 14. 788 61. 583 1. 00 34. 80 **ATOM** 2687 THR 376 35. 794 0 15. 901 61. 241 1. 00 32. 23 **ATOM** 2688 N ARG 377 37. 049 14.078 60. 848 1. 00 36. 51 ARG 377 **ATOM** 2689 CA 37. 523 14. 601 59. 581 1. 00 38. 20

- 237 -ATOM 2690 CB ARG 377 38. 535 58. 956 1.00 41.90 13. 640 ATOM 2691 CG ARG 377 39. 417 14. 271 57. 892 1. 00 43. 83 **ATOM** 2692 ARG 377 14. 280 CD 38. 735 56. 551 1. 00 46. 24 **ATOM** 2693 NE ARG 377 38. 467 12. 921 56. 074 1. 00 50. 02 ATOM 2694 CZARG 377 39. 400 12. 058 5 55. 679 1. 00, 48, 89 ATOM 2695 NH1 ARG 377 40.681 12. 405 55. 700 1. 00 47. 77 ATOM 2696 NH2 ARG 377 39. 050 10. 849 55. 256 1. 00 48. 65 2697 C ATOM ARG 377 36. 311 14. 759 58. 688 1. 00 37. 15 2698 ATOM 0 ARG 377 36. 163 15. 780 1. 00 37. 23 58. 016 ATOM 2699 N **ALA 378** 35. 445 13. 744 58. 706 1. 00 36. 43 10 ATOM 2700 ALA 378 34. 212 13. 732 CA 57. 920 1. 00 35. 58 ATOM 2701 CB ALA 378 33. 470 12. 430 58. 130 1. 00 35. 75 33. 314 2702 ATOM C ALA 378 14. 897 58. 304 1. 00 34. 75 2703 **ATOM** 0 ALA 378 32.675 15. 507 57. 451 1. 00 34. 63 ATOM 2704 N ALA 379 33. 249 15. 204 15 59. 590 1. 00 34. 17 2705 16. 317 MOTA CA ALA 379 32. 427 60.009 1. 00 34. 54 2706 32. 281 61.515 ATOM CBALA 379 16. 340 1. 00 32. 43 2707 33.073 ATOM C ALA 379 17. 607 59. 519 1. 00 35. 95 ATOM 2708 0 ALA 379 32. 465 18. 358 58. 761 1. 00 38. 27 ATOM 2709 N HIS 380 34. 314 17. 856 20 59. 925 1. 00 35. 13 34. 994 ATOM 2710 CA HIS 380 19.083 59. 526 1. 00 34. 04 ATOM 2711 CBHIS 380 36.448 19.031 59.968 1. 00 37. 01 ATOM 2712 CG HIS 380 36. 628 19. 284 61. 430 1. 00 42. 02 CD2 HIS 380 ATOM 2713 35. 734 19. 637 62. 385 1. 00 43. 27 ATOM 2714 ND1 HIS 380 37.852 25 19. 206 62.058 1. 00 44. 66 ATOM 2715 CE1 HIS 380 37.704 19.500 63. 339 1. 00 46. 06 NE2 HIS 380 ATOM 2716 36. 429 19. 766 63. 562 1. 00 44. 63 ATOM 2717 C HIS 380 34. 894 19. 405 58. 045 1. 00 32. 37 ATOM 2718 0 HIS 380 34. 581 20. 536 57. 671 1. 00 29. 98

- 238 -ATOM 2719 N MET 381 35. 154 18. 417 57. 197 1. 00 30. 55 2720 MET 381 ATOM CA 35. 055 18. 640 55. 764 1. 00 30. 35 2721 ATOM CBMET 381 35. 383 17. 365 54. 992 1. 00 28. 41 2722 CG MET 381 36.852 ATOM 17. 181 54. 767 1.00 28.31 2723 ATOM SD MET 381 37. 505 18.684 5 54. 017 1. 00 31. 73 ATOM 2724 CE MET 381 38. 142 18. 070 52. 446 1. 00 30. 02 2725 ATOM C MET 381 33. 647 19. 101 55. 415 1. 00 32. 29 **ATOM** 2726 0 MET 381 33. 453 19. 930 54. 527 1. 00 32. 42 ATOM 2727 CYS 382 32.660 N 18. 566 56. 124 1. 00 33. 02 **ATOM** 2728 CA CYS 382 31. 279 18. 942 10 55.869 1.00 33.44 ATOM 2729 CB CYS 382 30. 323 18. 012 56. 625 1. 00 33. 78 2730 CYS 382 **ATOM** SG 28. 582 18. 152 56. 124 1. 00 40. 21 2731 C **ATOM** CYS 382 31.087 20. 387 56. 316 1. 00 33. 02 **ATOM** 2732 0 CYS 382 30.566 21. 218 55. 563 1. 00 32. 71 2733 15 ATOM N SER 383 31. 528 20.686 57. 537 1.00 33.57 ATOM 2734 CA SER 383 1. 00 33. 39 31. 418 22. 037 58. 097 **ATOM** 2735 CB 32. 232 SER 383 22. 159 59. 392 1. 00 32. 88 ATOM 2736 0GSER 383 33. 605 21.877 59. 176 1. 00 31. 29 ATOM 2737 C SER 383 31. 935 23. 042 57. 085 1. 00 32. 50 20 **ATOM** 2738 0 SER 383 31. 314 24.073 56. 832 1. 00 32. 64 **ATOM** 2739 N ALA 384 33.082 22.729 56. 501 1. 00 30. 75 ATOM 2740 CAALA 384 33.663 23.607 55. 510 1.00 29.62 ATOM 2741 CB ALA 384 34. 787 22. 885 54. 789 1.00 29.04 ATOM 2742 C ALA 384 32.604 24. 095 54. 509 1. 00 29. 94 ATOM 2743 25 0 ALA 384 32. 211 25. 259 54. 544 1. 00 28. 35 ATOM 2744 N **GLY 385** 32. 141 23. 193 53. 639 1. 00 31. 38 ATOM 2745 CA **GLY 385** 31. 149 23. 525 52. 621 1.00 30.00 ATOM 2746 C GLY 385 29.870 24. 198 53. 090 1. 00 30. 54 ATOM 2747 0 GLY 385 29. 522 25. 285 52. 613 1. 00 28. 88

- 239 -1. 00 29. 58 **ATOM** 2748 N LEU 386 29. 151 23. 559 54. 010 **ATOM** 2749 CA LEU 386 27. 917 24. 148 54. 522 1. 00 28. 86 ATOM 2750 CBLEU 386 27. 410 23. 374 55. 749 1. 00 25. 55 LEU 386 ATOM 2751 CG 26. 141 23. 824 56. 493 1. 00 21. 28 2752 CD1 LEU 386 26.504 24. 768 ATOM 57. 605 1. 00 18. 56 5 ATOM 2753 CD2 LEU 386 25. 157 24. 456 55. 533 1. 00 17. 77 ATOM 2754 C LEU 386 28. 199 25. 595 54. 898 1. 00 30. 29 ATOM 2755 0 LEU 386 27. 344 26. 458 54. 728 1. 00 30. 86 ATOM 2756 ALA 387 29. 413 25. 846 N 55. 393 1. 00 32. 40 ATOM 2757 CA **ALA 387** 29.851 27. 184 55. 799 1. 00 32. 84 10 ATOM 2758 CBALA 387 31. 181 27. 101 56. 536 1. 00 31. 99 2759C 29. 991 ATOM ALA 387 28. 098 54. 585 1. 00 34. 20 2760 0 ATOM ALA 387 29. 509 29. 235 54. 588 1. 00 34. 34 **ATOM** 2761 N **GLY 388** 30.663 27. 597 53. 553 1. 00 34. 88 ATOM 2762 CA GLY 388 30. 831 28. 378 52. 344 1. 00 35. 13 15 ATOM 2763 C 29.467 28. 833 GLY 388 51.867 1. 00 35. 42 2764 ATOM 0 GLY 388 29. 257 30. 005 51. 545 1. 00 36. 39 ATOM 2765 N VAL 389 28. 524 27. 898 51.839 1. 00 34. 42 ATOM 2766 CA VAL 389 27. 167 28. 202 51. 402 1. 00 32. 28 ATOM 2767 CBVAL 389 26. 266 26. 949 20 51. 487 1. 00 31. 56 2768 CG1 VAL 389 24.856 27. 285 ATOM 51. 027 1. 00 28. 68 ATOM 2769 CG2 VAL 389 26.853 25. 836 50.638 1.00 28.05 ATOM 2770 C VAL 389 26. 579 29. 307 52. 273 1. 00 30. 86 ATOM 2771 VAL 389 26.072 30. 304 0 51. 762 1. 00 26. 91 2772 26.665 ATOM N ILE 390 29. 115 53. 586 25 1. 00 31. 06 2773 ILE 390 26. 146 30.073 **ATOM** CA 54. 548 1. 00 34. 83 **ATOM** 2774 CBILE 390 26. 262 29. 538 56.001 1. 00 32. 76 ATOM 2775 CG2 ILE 390 25. 733 30. 562 56. 996 1. 00 31. 45

2776

ATOM

CG1 ILE 390

25. 425

28. 274

56. 154 1. 00 32. 06

- 240 -ATOM CD1 ILE 390 25. 311 27. 804 57. 572 1. 00 31. 73 2777 1. 00 39. 01 ATOM 2778 C ILE 390 26.858 31. 415 54. 444 32. 465 54. 370 ILE 390 26. 209 1. 00 42. 11 ATOM 2779 0 2780 ASN 391 28. 186 31. 398 54. 437 1. 00 41. 07 ATOM N ASN 391 28. 921 32. 652 54. 326 1. 00 42. 97 ATOM 2781 CA 5 ATOM CB ASN 391 30.430 32. 386 54. 290 1.00 47.00 2782 ATOM 2783 CG ASN 391 31.061 32. 452 55. 678 1. 00 51. 32 OD1 ASN 391 32. 205 32. 029 55. 878 1. 00 51. 98 ATOM 2784 1. 00 51. 87 ATOM 2785 ND2 ASN 391 30. 312 32. 996 56. 646 1. 00 42. 59 C ASN 391 28. 459 33. 377 53. 070 **ATOM** 2786 10 ASN 391 27. 927 34. 488 53. 141 1. 00 40. 64 **ATOM** 2787 0 ARG 392 28.638 32. 723 51. 928 1. 00 43. 30 ATOM 2788 N 33. 277 1. 00 45. 75 **ATOM** 2789 CA ARG 392 28. 237 50. 644 ARG 392 28. 328 32. 182 49.571 1. 00 48. 20 **ATOM** 2790 CB 27. 020 31. 811 48. 892 1. 00 54. 22 **ATOM** 2791 CG ARG 392 15 1. 00 59. 36 ATOM 2792 CD ARG 392 26. 803 32. 578 47. 590 ATOM 2793 NE ARG 392 27. 491 31. 984 46. 437 1. 00 66. 46 2794 CZ ARG 392 28. 794 32. 098 46. 156 1. 00 69. 91 **ATOM** 29.613 32. 793 1. 00 69. 61 ATOM 2795 NH1 ARG 392 46. 941 29. 279 31. 524 ATOM 2796 NH2 ARG 392 45.063 1. 00 70. 50 20 26.822 ATOM 2797 C ARG 392 33. 854 50.711 1. 00 45. 30 2798 ARG 392 26.474 34. 777 1. 00 44. 35 ATOM 0 49. 973 MET 393 26.009 33. 316 1. 00 47. 21 **ATOM** 2799 N 51.607 2800 CA MET 393 24. 640 33. 785 51. 739 1. 00 50. 87 ATOM ATOM 2801 CB MET 393 23. 761 32. 687 52. 346 1. 00 49. 84 25 2802 CG MET 393 23. 427 31. 551 51. 389 1. 00 45. 97 ATOM ATOM 2803 SD MET 393 22. 244 30. 416 52.096 1. 00 42. 67 MET 393 20. 761 31. 465 52. 244 1. 00 42. 67 ATOM 2804 CE 2805 C 24. 559 52. 581 1. 00 54. 43 ATOM MET 393 35. 046

- 241 -**ATOM** 2806 0 MET 393 23. 631 35. 851 52. 443 1. 00 53. 85 1. 00 59. 09 ATOM 2807 N ARG 394 25. 528 35. 208 53. 469 ARG 394 25. 568 36. 386 54. 314 1.00 64.57 ATOM 2808 CA ATOM 2809 CB ARG 394 26.624 36. 224 55. 404 1.00 65.91 ARG 394 26.830 37, 477 56. 228 1. 00 67. 95 5 ATOM 2810 CG ATOM 2811 CD ARG 394 28. 048 37. 364 57. 130 1.00 69.02 ATOM 2812 NE ARG 394 28. 499 38. 673 57. 600 1. 00 68. 97 27. 776 39. 494 58. 357 1.00 69.21 ATOM 2813 CZ ARG 394 NH1 ARG 394 ATOM 2814 26. 553 39. 151 58. 743 1. 00 70. 35 NH2 ARG 394 28. 281 40.662 58.732 1.00 68.24 ATOM 2815 10 ATOM 2816 C ARG 394 25. 952 37. 537 53. 404 1.00 67.94 2817 ARG 394 25. 306 38. 588 53. 391 1.00 67.14 ATOM 0 2818 37. 313 52. 633 ATOM N GLU 395 27. 012 1. 00 72. 08 ATOM 2819 CA GLU 395 27. 513 38. 314 51. 707 1.00 77.04 2820 GLU 395 28. 578 37. 691 50.784 1.00 78.09 15 ATOM CB 2821 29. 425 38. 685 49. 955 1. 00 81. 99 ATOM CG GLU 395 2822 GLU 395 30. 402 39. 533 50. 789 1.00 84.19 ATOM CD 2823 0E1 GLU 395 29.949 40. 442 51. 526 1.00 83.64 ATOM ATOM 2824 0E2 GLU 395 31. 631 39. 290 50. 702 1. 00 84. 22 ATOM 2825 26. 340 38. 873 C GLU 395 50.898 1. 00 79. 30 20 2826 26. 250 ATOM 0 GLU 395 40.078 50.683 1. 00 81. 15 ATOM 2827 N SER 396 25. 423 38. 007 50.481 1. 00 81. 59 ATOM 2828 CA SER 396 24. 276 38. 451 49.696 1. 00 83. 40 23. 379 ATOM 2829 CB SER 396 37. 264 49. 366 1. 00 84. 05 2830 SER 396 24. 123 36. 252 48. 716 1. 00 86. 28 25 ATOM 0G 39. 526 **ATOM** 2831 C SER 396 23. 462 50.406 1. 00 84. 36 ATOM 2832 0 SER 396 23. 578 40. 708 50.092 1. 00 84. 49 ATOM 2833 N 22. 639 39. 118 1. 00 86. 41 ARG 397 51. 362 ATOM 2834 CA ARG 397 21.812 40.070 52. 090 1. 00 88. 71

- 242 -ARG 397 20.682 39. 335 52. 816 1.00 89.74 ATOM 2835 CB1.00 90.87 **ATOM** 2836 CG ARG 397 19. 579 40. 241 53. 346 39. 776 1.00 91.04 ARG 397 19.096 54. 713 **ATOM** 2837 CD ATOM 2838 NE ARG 397 20.021 40. 158 55. 782 1. 00 89. 87 39.766 1. 00 89. 80 CZARG 397 19. 905 57. 047 ATOM 2839 5 NH1 ARG 397 18.906 38.971 57. 409 1. 00 91. 15 ATOM 2840 NH2 ARG 397 2841 20.779 40. 174 57. 955 1. 00 87. 97 ATOM 1. 00 89. 74 C ARG 397 22.653 40. 847 53. 102 ATOM 2842 22. 585 40. 588 54. 305 1. 00 90. 41 **ATOM** 2843 0 ARG 397 1.00 90.58 **SER 398** 23. 448 41. 795 52. 614 ATOM 2844 N 10 SER 398 24. 288 42.602 53. 492 1.00 91.09 ATOM 2845 CA SER 398 24. 903 43. 782 52. 718 1.00 91.14 2846 CB ATOM 1. 00 89. 49 ATOM 2847 0G SER 398 25. 845 43. 347 51. 747 2848 SER 398 23. 470 43. 129 54.677 1. 00 91. 27 ATOM C 43.810 1.00 91.10 ATOM 2849 0 SER 398 22. 458 54. 496 15 23. 904 42. 786 55. 887 1.00 91.43 ATOM 2850 N GLU 399 23. 238 43. 233 57. 108 1. 00 90. 89 ATOM 2851 CA GLU 399 21. 799 42. 705 57. 183 1. 00 91. 87 2852 CB GLU 399 ATOM 2853 CG **GLU 399** 20. 969 43. 349 58. 298 1. 00 93. 31 ATOM 20. 726 44. 836 1. 00 94. 22 2854 CD GLU 399 58.064 ATOM 20 20. 270 45. 533 0E1 GLU 399 58. 999 1. 00 93. 53 ATOM 2855 0E2 GLU 399 20. 986 45. 307 56. 936 1. 00 94. 80 **ATOM** 2856 2857 C GLU 399 24. 013 42. 774 58. 339 1. 00 89. 25 ATOM 2858 GLU 399 24. 987 42.029 58. 236 1. 00 88. 96 ATOM 0 23. 570 43. 226 1. 00 87. 38 25 ATOM 2859 N ASP 400 59. 502 1. 00 85. 70 2860 ASP 400 24. 214 42. 883 60. 754 ATOM CA 2861 23. 332 43. 352 61. 915 1. 00 88. 35 ATOM CBASP 400 22. 861 44. 795 61. 743 1.00 90.64 ATOM 2862 CG ASP 400 ATOM 2863 OD1 ASP 400 22. 059 45. 055 60.817 1. 00 91. 42

- 243 -ATOM OD2 ASP 400 23. 297 45. 671 62. 524 1. 00 91. 68 2864 41. 385 60.853 1. 00 82. 94 ATOM 2865 C ASP 400 24. 496 25. 506 40.900 60. 346 1. 00 82. 03 ASP 400 ATOM 2866 0 ATOM 2867 N VAL 401 23. 593 40.658 61. 502 1. 00 79. 90 39. 219 61.682 1. 00 75. 91 VAL 401 23. 738 ATOM 2868 CA 5 **ATOM** 2869 CB VAL 401 23.607 38. 841 63. 153 1. 00 74. 20 1. 00 73. 12 ATOM 2870 CG1 VAL 401 24. 803 39. 343 63. 927 22. 314 39. 430 63. 710 1. 00 72. 79 CG2 VAL 401 ATOM 2871 22.662 38. 458 60. 925 1. 00 74. 63 ATOM 2872 C VAL 401 1. 00 75. 56 2873 21. 489 38. 846 60. 942 ATOM 0 VAL 401 10 MET 402 23.063 37. 365 60. 278 1. 00 70. 61 **ATOM** 2874 N 2875 22. 130 36. 539 59. 521 1. 00 65. 65 ATOM CA MET 402 22.818 1. 00 62. 74 ATOM 2876 CB MET 402 35. 887 58. 325 21.897 34. 958 1. 00 56. 61 2877 CG MET 402 57. 543 ATOM 2878 22. 543 34. 551 55. 906 1. 00 52. 49 15 ATOM SD MET 402 2879 23.857 33. 399 56. 323 1. 00 49. 76 ATOM CE MET 402 2880 21. 532 35. 450 60. 381 1. 00 65. 00 ATOM C MET 402 22. 222 34. 513 60. 781 1. 00 65. 18 2881 0 MET 402 ATOM 2882 N ARG 403 20. 241 35. 575 60. 657 1. 00 63. 62 ATOM 19.535 34. 593 61.462 2883 CA ARG 403 1. 00 61. 57 ATOM 20 18. 418 35. 275 62. 262 2884 CB ARG 403 1. 00 64. 83 ATOM 2885 ARG 403 18.856 36. 547 62. 987 1. 00 70. 01 ATOM CG 2886 CDARG 403 17. 691 37. 205 63. 724 1. 00 75. 36 ATOM 36. 582 2887 NE ARG 403 17. 412 65. 018 1. 00 80. 50 ATOM 2888 16. 305 36. 788 65. 731 1. 00 83. 41 25 ATOM CZARG 403 65. 277 1. 00 84. 55 2889 NH1 ARG 403 15. 358 37. 603 ATOM NH2 ARG 403 16. 147 36. 187 66. 907 1. 00 83. 64 ATOM 2890 18. 946 33. 560 60. 504 1. 00 57. 99 ATOM 2891 C ARG 403 60. 135 1. 00 58. 57 MOTA 2892 0 ARG 403 17. 775 33. 639

- 244 -19. 762 32. 597 60. 091 1. 00 52. 97 ATOM ILE 404 2893 N 59. 170 1. 00 49. 14 ATOM 2894 CA ILE 404 19. 301 31. 570 57. 999 1. 00 47. 44 20. 293 31. 412 ATOM 2895 CB ILE 404 21. 538 30.680 58. 458 1. 00 43. 94 CG2 ILE 404 ATOM 2896 56. 854 1. 00 48. 45 CG1 ILE 404 19.629 30.649 **ATOM** 2897 5 30. 559 55. 598 1. 00 48. 95 CD1 ILE 404 20. 477 ATOM 2898 19. 126 30. 222 59.879 1. 00 48. 34 ATOM 2899 C ILE 404 29. 967 60. 897 1. 00 48. 83 19. 771 ATOM 2900 0 ILE 404 1.00 46.42 THR 405 18. 236 29. 380 59. 346 ATOM 2901 N 59.892 1. 00 42. 37 17. 956 28. 043 **ATOM** 2902 CA THR 405 10 60. 222 1.00 41.93 CBTHR 405 16.451 27. 838 ATOM 2903 1. 00 43. 89 OG1 THR 405 16.010 28. 839 61. 145 ATOM 2904 1. 00 38. 85 CG2 THR 405 16. 227 26. 475 60. 849 ATOM 2905 26. 990 58. 857 1. 00 39. 95 THR 405 18. 332 ATOM 2906 C 1. 00 38. 97 ATOM 2907 0 THR 405 18. 178 27. 204 57. 653 15 1. 00 38. 10 18. 809 25. 844 59. 324 ATOM 2908 N VAL 406 CA VAL 406 19. 195 24. 776 58. 414 1. 00 36. 64 ATOM 2909 20.686 24. 442 58. 563 1. 00 35. 12 VAL 406 ATOM 2910 CB 23. 342 57.600 1. 00 35. 29 ATOM 2911 CG1 VAL 406 21.069 25. 672 1. 00 35. 40 CG2 VAL 406 21. 515 58. 303 ATOM 2912 20 23.499 1. 00 35. 83 2913 C VAL 406 18. 390 58. 635 ATOM 18. 214 23.058 59. 765 1. 00 37. 06 2914 0 VAL 406 ATOM 17.895 22. 915 57. 549 1. 00 34. 50 **ATOM** 2915 N **GLY 407** 17. 143 21. 680 57. 653 1. 00 32. 79 **GLY 407** ATOM 2916 CA 1. 00 32. 90 ATOM 2917 C **GLY 407** 18.074 20. 522 57. 353 25 18.704 20.467 56. 294 1. 00 33. 85 2918 **GLY 407** ATOM 0 1. 00 31. 27 2919 N VAL 408 18. 177 19. 585 58. 279 ATOM 19.064 18. 466 58. 054 1. 00 29. 57 ATOM 2920 CA VAL 408 20. 199 18. 491 59. 042 1.00 29.66 ATOM 2921 CBVAL 408

- 245 -17. 767 58. 468 1.00 31.77 CG1 VAL 408 21. 390 **ATOM** 2922 1. 00 29. 91 ATOM 2923 CG2 VAL 408 20. 515 19. 916 59. 412 58. 206 1. 00 29. 58 18. 366 17. 135 **ATOM** 2924 C VAL 408 17. 392 17.015 58. 942 1. 00 28. 54 VAL 408 ATOM 2925 0 57. 509 1. 00 30. 15 ASP 409 18.878 16. 131 ATOM 2926 N 5 14. 789 57. 598 1. 00 31. 95 ASP 409 18. 324 ATOM 2927 CA 17. 109 14. 635 56. 674 1. 00 35. 66 **ATOM** 2928 CB ASP 409 1. 00 40. 01 13. 252 56. 775 ASP 409 16. 455 ATOM 2929 CG 12. 928 55. 898 1. 00 40. 26 **ATOM** 2930 OD1 ASP 409 15. 613 57. 728 1.00 39.33 12. 499 OD2 ASP 409 16. 773 **ATOM** 2931 10 13. 824 57. 180 1.00 31.91 **ATOM** 2932 C ASP 409 19. 415 1. 00 32. 39 14. 208 56. 484 ASP 409 20. 352 ATOM 2933 0 57. 607 1.00 31.09 ATOM 2934 N GLY 410 19. 300 12. 574 1. 00 29. 56 11. 593 57. 233 GLY 410 20. 299 ATOM 2935 CA 10.704 58.385 1. 00 29. 32 2936 C **GLY 410** 20.703 ATOM 15 59. 558 1. 00 28. 27 20. 510 11. 041 ATOM 2937 0 GLY 410 1. 00 28. 24 N SER 411 21. 282 9. 559 58. 053 ATOM 2938 1. 00 27. 52 8. 631 59.086 SER 411 21. 699 ATOM 2939 CA 7. 253 58. 481 1.00 29.46 **ATOM** 2940 CB SER 411 22.018 7. 316 57. 471 1. 00 31. 64 23. 016 ATOM 2941 0G SER 411 20 9.160 1. 00 25. 78 C SER 411 22. 895 59. 863 ATOM 2942 1. 00 25. 89 9. 113 61.090 SER 411 22. 909 ATOM 2943 0 23.890 9.687 59. 161 1. 00 23. 18 2944 N VAL 412 ATOM 10. 185 59. 839 1. 00 21. 25 VAL 412 25. 076 **ATOM** 2945 CA 1. 00 20. 56 2946 VAL 412 26. 099 10.669 58. 841 ATOM CB 25 1. 00 17. 73 27. 372 11. 084 59. 564 2947 CG1 VAL 412 ATOM 1.00 20.59 CG2 VAL 412 26.378 9. 552 57. 857 ATOM 2948 24. 769 11. 300 1. 00 20. 44 ATOM 2949 C VAL 412 60. 818

25. 182

ATOM

2950

0

VAL 412

61. 983

11. 262

1. 00 21. 51

- 246 -1. 00 16. 42 24. 033 12. 288 60. 340 ATOM 2951 N TYR 413 61. 171 ATOM 2952 CA TYR 413 23.659 13. 409 1. 00 16. 41 14. 526 60. 288 1. 00 16. 40 ATOM 2953 CBTYR 413 23. 095 22. 700 15. 762 61.051 1. 00 14. 37 TYR 413 ATOM 2954 CG CD1 TYR 413 61. 434 1. 00 13. 43 23. 645 16. 707 5 ATOM 2955 17. 789 62. 226 1. 00 13. 93 CE1 TYR 413 23. 296 ATOM 2956 21.401 15. 939 61. 470 1. 00 13. 10 **ATOM** 2957 CD2 TYR 413 1. 00 15. 82 17. 007 62. 256 CE2 TYR 413 21. 049 ATOM 2958 1. 00 14. 65 ATOM CZTYR 413 21. 994 17. 927 62. 638 2959 63. 475 1. 00 16. 02 21.620 18. 948 ATOM 2960 OH TYR 413 10 1. 00 17. 41 ATOM 2961 C TYR 413 22.626 13.007 62. 233 1. 00 18. 36 22. 364 13. 758 63. 172 ATOM 2962 0 TYR 413 ATOM 2963 N LYS 414 22. 035 11.826 62. 103 1. 00 18. 12 1.00 19.00 21.033 11. 426 63. 083 ATOM 2964 CA LYS 414 2965 CBLYS 414 19.706 11. 130 62. 384 1. 00 19. 22 ATOM 15 1. 00 18. 92 18.962 12. 358 61. 894 ATOM 2966 CG LYS 414 CD LYS 414 17.615 11. 965 61. 314 1. 00 21. 36 ATOM 2967 1.00 25.08 CE 16.829 13. 181 60.855 **ATOM** LYS 414 2968 12.829 1. 00 28. 46 ATOM 2969 NZ LYS 414 15. 567 60. 132 10. 249 1. 00 20. 50 21. 400 63. 975 20 ATOM 2970 C LYS 414 9.883 1. 00 21. 27 2971 0 LYS 414 20.637 64. 871 ATOM 9.655 1. 00 22. 22 22. 565 63. 753 2972 N LEU 415 ATOM 8. 511 64. 565 1. 00 23. 27 ATOM 2973 CA LEU 415 22. 958 1. 00 21. 47 LEU 415 22. 679 7. 218 63. 784 ATOM 2974 CB 2975 CG LEU 415 21. 234 6.978 63. 313 1. 00 17. 45 ATOM 25 1.00 16.66 21. 158 5. 672 62. 545 ATOM 2976 CD1 LEU 415 CD2 LEU 415 20. 293 6.954 64. 498 1. 00 14. 44 ATOM 2977 1. 00 25. 05 **ATOM** 2978 C LEU 415 24. 418 8. 566 65. 033 1. 00 26. 05 29790 24. 921 7. 625 65. 657 ATOM LEU 415

- 247 -ATOM 2980 N HIS 416 25. 095 9. 673 64. 736 1.00 24.04 ATOM 2981 CA HIS 416 26. 481 9.852 65. 147 1. 00 22. 40 ATOM 2982 CB HIS 416 27. 365 9. 997 63. 922 1. 00 23. 29 ATOM 2983 CG HIS 416 27. 383 8. 774 63.069 1. 00 25. 75 5 ATOM 2984 CD2 HIS 416 28. 392 7. 937 62. 729 1. 00 27. 82 ATOM 2985 ND1 HIS 416 26. 241 62. 506 8. 248 1.00 26.69 **ATOM** 2986 CE1 HIS 416 26. 545 7. 138 61.857 1. 00 28. 69 ATOM NE2 HIS 416 2987 27.844 6.926 61. 977 1. 00 28. 20 ATOM 2988 C HIS 416 26. 577 11.080 66. 027 1. 00 21. 63 ATOM HIS 416 10 2989 0 26.808 12. 184 65. 558 1.00 22.44 ATOM 2990 N PRO 417 26. 386 10. 898 67. 331 1. 00 21. 25 ATOM 2991 CD PRO 417 26. 126 9. 627 68. 015 1. 00 22. 18 ATOM 2992 CA PRO 417 26. 440 11. 991 68. 297 1. 00 22. 07 ATOM 2993 CB PRO 417 26. 447 11. 258 69. 627 1. 00 21. 52 ATOM 2994 CG 15 PRO 417 25. 565 10. 108 69. 340 1. 00 23. 41 ATOM 2995 C PRO 417 27. 655 12. 874 68. 113 1. 00 22. 46 ATOM 2996 0 PRO 417 27.519 14.076 67.878 1. 00 22. 18 ATOM 2997 N SER 418 28. 835 12. 262 68. 221 1. 00 20. 96 **ATOM** 2998 CA SER 418 30. 105 12. 959 68. 064 1. 00 18. 32 ATOM 20 2999 CBSER 418 31. 264 11. 962 68. 076 1. 00 20. 88 ATOM 3000 0G SER 418 32. 419 12. 512 67. 460 1.00 24.12 ATOM 3001 C SER 418 30. 099 13. 720 66. 757 1.00 15.71 ATOM 3002 0 SER 418 30. 269 14. 935 66. 742 1. 00 16. 10 ATOM 3003 N PHE 419 29.905 13. 010 65. 656 1. 00 11. 39 ATOM 25 3004 CA PHE 419 29.864 13. 683 64. 379 1. 00 10. 22 **ATOM** 3005 CB PHE 419 29. 243 12. 789 63. 335 1. 00 5. 53 ATOM 3006 CG PHE 419 29. 035 13. 468 62. 034 1. 00 1. 42 ATOM 3007 CD1 PHE 419 29. 814 13. 137 60. 942 1.00 3. 13 ATOM 3008 CD2 PHE 419 28.080 14. 449 61. 893 1.00 1.00

- 248 -1.00 1. 47 CE1 PHE 419 29.648 13. 773 59. 712 ATOM 3009 **ATOM** CE2 PHE 419 27. 909 15.088 60.670 1.00 2. 68 3010 14. 746 59. 575 1.00 1.00 ATOM CZPHE 419 28. 699 3011 1. 00 12. 48 29.037 14. 965 64. 472 C PHE 419 ATOM 3012 1. 00 12. 11 29. 520 16. 048 64. 156 ATOM 3013 0 PHE 419 5 64. 900 1. 00 15. 88 LYS 420 27. 785 14. 838 ATOM 3014 N 64. 994 1. 00 20. 63 **ATOM** CA LYS 420 26.917 16.000 3015 1. 00 21. 26 25. 525 15. 610 65. 522 ATOM 3016 CBLYS 420 24. 470 16. 730 65. 361 1. 00 22. 35 ATOM CG LYS 420 3017 1.00 22.81 23. 045 16. 288 65. 686 **ATOM** CD LYS 420 10 3018 LYS 420 22. 942 15. 740 67. 102 1. 00 25. 24 ATOM 3019 CE 15. 092 67. 350 1. 00 27. 51 **ATOM** 3020 NZ LYS 420 21.616 C LYS 420 27. 505 17. 099 65. 866 1. 00 24. 04 ATOM 3021 1. 00 23. 74 LYS 420 27. 533 18. 260 65. 465 **ATOM** 3022 0 1. 00 29. 67 3023 N GLU 421 27. 978 16. 733 67. 053 **ATOM** 15 1. 00 34. 96 17. 701 67. 999 **ATOM** 3024 CAGLU 421 28. 550 29. 075 16. 972 69. 244 1. 00 36. 76 ATOM 3025 CBGLU 421 29. 292 17.843 70. 480 1. 00 40. 52 ATOM 3026 CG GLU 421 17. 047 1. 00 43. 55 ATOM 3027 CD GLU 421 29.895 71. 638 30. 981 16. 467 71. 445 1. 00 47. 03 ATOM 3028 OE1 GLU 421 20 0E2 GLU 421 29. 294 16.990 72. 734 1. 00 43. 28 ATOM 3029 29.680 18. 512 67. 369 1.00 36.40 C GLU 421 ATOM 3030 29.689 19. 745 1. 00 38. 37 ATOM 3031 0 GLU 421 67. 442 17. 816 66. 751 1.00 35.66 ARG 422 30.629 ATOM 3032 N 1. 00 35. 13 ATOM 3033 CA ARG 422 31. 755 18. 477 66. 124 25 1. 00 38. 76 ARG 422 32. 801 17. 449 65. 684 ATOM 3034 CB16. 525 1. 00 46. 51 ATOM 3035 CG ARG 422 33. 277 66. 811 17. 286 1. 00 51. 67 ARG 422 33. 915 67. 980 ATOM 3036 CD 35. 322 17. 578 67. 732 1. 00 57. 41 ATOM 3037 NE ARG 422

- 249 -1.00 60.70 ARG 422 36. 269 16.649 67. 625 CZ ATOM 3038 1. 00 60. 82 15. 364 67. 749 **ATOM** 3039 NH1 ARG 422 35. 956 1.00 61.68 17.002 67. 380 37. 529 ATOM 3040 NH2 ARG 422 64.942 1. 00 33. 47 ARG 422 31.256 19. 278 С ATOM 3041 1.00 35.28 64.803 31.585 20.450 ARG 422 ATOM 3042 0 5 30. 446 18. 654 64. 096 1. 00 32. 46 PHE 423 ATOM 3043 N 1. 00 30. 30 29. 901 19. 348 62. 930 ATOM CA PHE 423 3044 62. 165 1. 00 27. 32 18. 423 PHE 423 28. 949 **ATOM** 3045 CB 1. 00 23. 75 61.063 PHE 423 28. 188 19. 106 ATOM 3046 CG 61. 270 1. 00 22. 33 26.891 19. 552 CD1 PHE 423 ATOM 3047 10 1. 00 23. 98 28.765 19. 293 59. 814 ATOM 3048 CD2 PHE 423 1. 00 22. 83 60. 245 26. 178 20. 169 ATOM CE1 PHE 423 3049 58. 784 1. 00 22. 46 28.061 19. 909 CE2 PHE 423 ATOM 3050 59. 001 1. 00 22. 73 26.769 20. 347 CZPHE 423 ATOM 3051 1. 00 29. 75 20.663 63. 280 3052 C PHE 423 29. 185 ATOM 15 62. 568 1. 00 27. 58 29. 328 21. 652 PHE 423 ATOM 3053 0 1.00 30.19 20.694 64. 363 3054 N HIS 424 28. 415 ATOM 21. 936 64. 692 1. 00 32. 48 27. 743 HIS 424 ATOM 3055 CA 1. 00 32. 75 26. 754 21. 760 65. 835 **ATOM** 3056 CBHIS 424 21. 279 65. 387 1. 00 31. 94 25. 412 HIS 424 ATOM 3057 CG 20 1.00 29.85 20.860 64. 176 24. 980 3058 CD2 HIS 424 ATOM 24. 341 21. 147 66. 243 1. 00 32. 28 ND1 HIS 424 **ATOM** 3059 1.00 30.67 CE1 HIS 424 23. 308 20.661 65. 580 **ATOM** 3060 1. 00 30. 19 23. 670 20. 477 64. 323 NE2 HIS 424 ATOM 3061 1. 00 35. 15 28. 737 23.011 65. 048 3062 C HIS 424 ATOM 25 1. 00 36. 91 28.689 24. 102 64. 487 HIS 424 ATOM 3063 0 22.711 65. 979 1. 00 36. 32 3064 N ALA 425 29.636 ATOM 1.00 36.74 30. 652 23. 675 66. 395 **ATOM** 3065 CA ALA 425

31. 542

ATOM

3066

CB

ALA 425

23. 058

67. 444

1. 00 35. 43

- 250 -**ATOM** 65. 201 1. 00 37. 82 3067 C -ALA 425 31. 492 24. 149 ALA 425 **ATOM** 3068 0 31. 420 25. 316 64. 809 1. 00 38. 66 32. 274 23. 243 64. 617 1. 00 37. 75 ATOM 3069 N SER 426 23. 576 63. 466 1. 00 37. 83 ATOM 3070 CA SER 426 33. 113 1. 00 38. 67 SER 426 33. 602 22. 289 62. 782 5 ATOM 3071 CB 1. 00 37. 85 **ATOM** SER 426 34. 440 22. 560 61.667 3072 0G 62. 445 1. 00 37. 21 **ATOM** 3073 C SER 426 32. 390 24. 461 1.00 37.08 SER 426 33. 025 25. 151 61. 657 ATOM 3074 0 **ATOM** 3075 N VAL 427 31. 064 24. 443 62. 450 1. 00 37. 84 1. 00 38. 87 ATOM CA VAL 427 30. 321 25. 269 61. 510 10 3076 1. 00 39. 38 ATOM 3077 CBVAL 427 28. 935 24.667 61. 194 1.00 37.50 CG1 VAL 427 25. 744 60. 633 ATOM 3078 28. 000 ATOM CG2 VAL 427 29. 092 23. 534 60. 188 1. 00 36. 83 3079 C 30. 138 26. 655 62.090 1. 00 39. 54 ATOM 3080 VAL 427 ATOM 3081 0 VAL 427 30. 578 27. 639 61. 512 1. 00 40. 58 15 26. 724 63. 238 1. 00 40. 14 ATOM 3082 N ARG 428 29. 483 ATOM 3083 ARG 428 29. 247 27. 993 63. 897 1. 00 42. 86 CA 27. 739 1. 00 42. 72 **ATOM** 28. 603 65. 258 3084 CB ARG 428 **ATOM** 3085 CG ARG 428 27. 288 26. 982 65. 186 1. 00 43. 31 ATOM ARG 428 27. 139 26. 044 66. 378 1. 00 46. 03 20 3086 CD ATOM 3087 NE ARG 428 25. 802 25. 461 66. 485 1. 00 47. 83 CZ24.690 26. 173 1. 00 48. 39 ATOM 3088 ARG 428 66. 648 24. 757 27. 499 1.00 47.35 **ATOM** 3089 NH1 ARG 428 66. 716 1. 00 47. 34 ATOM 3090 NH2 ARG 428 23. 516 25. 559 66. 756 ATOM 3091 C ARG 428 30. 561 28. 768 64.064 1. 00 44. 67 25 30.001 1. 00 45. 05 3092 0 ARG 428 30. 577 64.060 ATOM **ATOM** 3093 N ARG 429 31.663 28. 037 64. 195 1. 00 45. 77 32. 972 28. 652 1. 00 46. 48 ATOM 3094 CA ARG 429 64. 378 CB27. 738 65. 244 1. 00 52. 63 ATOM 3095 ARG 429 33. 849

- 251 -**ATOM** 3096 CG ARG 429 33. 260 27. 471 66. 648 1.00 59.36 ATOM 3097 CD ARG 429 33. 828 26. 199 67. 328 1. 00 64. 53 ATOM ARG 429 26. 286 3098 NE 35. 247 67. 677 1. 00 66. 23 CZARG 429 35.963 25. 274 ATOM 3099 68. 159 1. 00 66. 80 ATOM 3100 NH1 ARG 429 35. 398 24.083 68. 357 5 1. 00 66. 02 NH2 ARG 429 1.00 68.38 ATOM 3101 37. 249 25. 455 68. 435 ATOM 3102 C 33.657 28. 954 ARG 429 63.049 1.00 44.06 ATOM 3103 0 ARG 429 34. 885 28. 943 62. 954 1. 00 43. 92 ATOM 3104 N LEU 430 32. 847 29. 221 62. 029 1. 00 41. 46 10 ATOM 3105 CA LEU 430 33. 333 29. 551° 60.692 1. 00 40. 12 ATOM 3106 CBLEU 430 33. 495 28. 300 59. 830 1. 00 35. 57 3107 LEU 430 ATOM CG 34. 755 27. 468 60. 042 1. 00 34. 48 ATOM 3108 CD1 LEU 430 34. 764 26. 279 1. 00 32. 77 59. 101 **ATOM** 3109 CD2 LEU 430 35.965 28. 332 59. 806 1. 00 33. 57 15 ATOM 3110 C LEU 430 32. 332 30. 468 60. 029 1. 00 42. 10 58. 880 1. 00 42. 67 ATOM 3111 0 LEU 430 32. 503 30. 868 ATOM 3112 N THR 431 31. 280 30. 797 60. 763 1. 00 44. 70 3113 CA 30. 238 31.658 ATOM THR 431 60. 239 1. 00 48. 98 ATOM 3114 CBTHR 431 28. 923 30.928 60. 113 1. 00 49. 80 ATOM 3115 OG1 THR 431 28. 533 30. 463 20 61. 410 1. 00 50. 69 ATOM 3116 CG2 THR 431 29. 048 29. 758 59. 159 1.00 51.11 3117 29.999 32.820 **ATOM** C THR 431 61. 174 1.00 51.66 **ATOM** 3118 0 THR 431 28.986 32.868 61.881 1. 00 52. 07 ATOM 3119 30.935 N PRO 432 33. 774 61. 190 1. 00 52. 95 ATOM 3120 CD PRO 432 32. 179 33. 719 25 60. 403 1. 00 51. 90 3121 30.886 ATOM CA PRO 432 34. 980 62. 020 1. 00 52. 47 **ATOM** 3122 CBPRO 432 32. 135 35. 733 61. 587 1. 00 54. 48 PRO 432 ATOM 3123 CG 33. 073 34. 623 61. 176 1. 00 54. 21 ATOM 3124 C PRO 432 29.620 35. 783 61. 739 1. 00 52. 15

- 252 -**ATOM** 3125 0 PRO 432 29. 257 35. 981 60. 582 1. 00 49. 70 ATOM 3126 N SER 433 28. 955 36. 243 62. 793 1. 00 53. 82 SER 433 27. 734 37. 042 ATOM 3127 CA 62. 652 1. 00 57. 56 **ATOM** 3128 CB SER 433 28.055 38. 372 61. 952 1. 00 59. 89 28.537 5 ATOM 3129 0G SER 433 38. 176 60. 633 1. 00 62. 34 **ATOM** 3130 C **SER 433** 26.570 36. 340 61.926 1. 00 57. 57 ATOM 3131 0 SER 433 25. 907 36. 923 61.056 1. 00 57. 63 3132 CYS 434 26. 327 35. 088 62. 306 ATOM N 1. 00 56. 67 ATOM 3133 CA CYS 434 25. 256 34. 275 61. 738 1. 00 54. 67 ATOM 3134 CB25.805 33. 375 CYS 434 60. 634 1. 00 54. 21 10 34. 213 **ATOM** 3135 SG CYS 434 26. 729 59. 354 1. 00 55. 95 ATOM 3136 C CYS 434 24. 657 33. 390 62. 832 1. 00 54. 71 ATOM 3137 0 CYS 434 25. 381 32. 663 63. 513 1. 00 54. 74 ATOM 3138 23. 344 33. 454 N GLU 435 63. 011 1.00 54.63 3139 15 ATOM CA GLU 435 22. 681 32. 621 64.009 1. 00 54. 57 21. 529 64. 681 ATOM 3140 CB GLU 435 33. 383 1. 00 59. 73 ATOM 3141 CG GLU 435 21. 927 34. 615 65. 511 1. 00 64. 17 3142 CD GLU 435 20.717 35. 479 ATOM 65. 902 1. 00 67. 96 3143 0E1 GLU 435 20.905 36. 554 ATOM 66. 521 1. 00 68. 24 ATOM 3144 0E2 GLU 435 19. 574 20 35. 079 65. 584 1. 00 69. 98 3145 22. 134 ATOM C GLU 435 31. 378 63. 289 1. 00 51. 70 3146 21.058 ATOM 0 **GLU 435** 31. 412 62. 685 1. 00 51. 14 ATOM 3147 N ILE 436 22. 889 30. 288 63.350 1.00 47.61 22. 497 29. 046 ATOM 3148 CA ILE 436 62. 702 1. 00 43. 09 23.719 25 ATOM 3149 CB ILE 436 28. 331 62. 118 1. 00 38. 65 3150 CG2 ILE 436 23. 278 27. 138 ATOM 61.300 1. 00 38. 13 24. 502 29. 286 ATOM 3151 CG1 ILE 436 61. 234 1. 00 34. 79 1. 00 34. 08 ATOM 3152 CD1 ILE 436 25. 768 28. 686 60. 710 ATOM 3153 C 21. 798 28. 088 63. 664 1. 00 42. 96 ILE 436

- 253 -ATOM 3154 0 ILE 436 22. 403 27. 608 64.621 1.00 43.46 ATOM 3155 N THR 437 20. 521 27. 821 63. 402 1. 00 41. 73 ATOM 3156 CA THR 437 19. 724 26. 910 64. 218 1. 00 39. 10 ATOM CB THR 437 3157 18. 384 27. 553 64.638 1.00 37.86 ATOM 3158 OG1 THR 437 5 18. 182 28. 763 63.899 1. 00 37. 22 CG2 THR 437 ATOM 3159 18. 370 27.856 66. 130 1.00 37.07 ATOM C THR 437 3160 19. 430 25. 672 63. 380 1. 00 38. 74 ATOM 3161 0 THR 437 18. 979 25. 784 62. 238 1. 00 39. 10 ATOM 3162 N PHE 438 19.696 24. 494 63. 936 1. 00 36. 24 ATOM 3163 CA PHE 438 23. 257 10 19. 449 63. 210 1. 00 33. 18 ATOM 3164 CBPHE 438 20. 556 22. 256 63. 491 1. 00 30. 88 **ATOM** 3165 CG PHE 438 21. 905 22. 742 63.093 1. 00 32. 48 **ATOM** 3166 CD1 PHE 438 22. 597 23. 652 63.887 1. 00 31. 95 ATOM 3167 CD2 PHE 438 22. 489 22. 301 61. 913 1. 00 32. 85 ATOM 15 3168 CE1 PHE 438 23. 857 24. 118 63. 507 1. 00 31. 30 ATOM 3169 CE2 PHE 438 23. 745 22. 758 61. 522 1. 00 32. 28 ATOM 3170 CZPHE 438 24. 432 23. 668 62.320 1. 00 31. 80 ATOM 3171 C PHE 438 18. 102 22. 648 63.563 1. 00 33. 15 ATOM 3172 PHE 438 0 17. 662 22. 729 64.705 1. 00 '34. 90 20 ATOM 3173 N ILE 439 17. 450 22. 049 62.570 1. 00 31. 06 ATOM CA 3174 ILE 439 16. 150 21. 412 62. 738 1. 00 28. 59 ATOM 3175 CB ILE 439 15.010 22. 347 62. 321 1.00 26.74 ATOM CG2 ILE 439 3176 15. 268 22. 879 60. 937 1. 00 27. 91 ATOM 3177 CG1 ILE 439 13. 683 21. 591 62. 312 1. 00 27. 91 25 **ATOM** 3178 CD1 ILE 439 12. 545 22. 406 61.776 1.00 26.70 ATOM 3179 C ILE 439 16. 113 20. 190 61.837 1. 00 29. 76 ATOM 3180 0 ILE 439 16. 208 20. 310 60.618 1. 00 29. 55 ATOM 3181 N GLU 440 15. 977 19. 014 62. 434 1. 00 30. 76 **ATOM** 3182 CA GLU 440 15. 934 17. 781 61.666 1. 00 32. 34

- 254 -ATOM 3183 CB**GLU 440** 16. 028 16. 592 62. 609 1. 00 34. 09 ATOM 3184 CG GLU 440 17. 272 16. 583 63. 458 1. 00 38. 93 ATOM 3185 CD GLU 440 17. 339 15. 367 64. 353 1. 00 43. 10 0E1 GLU 440 15. 162 65. 131 1. 00 44. 22 ATOM 3186 16.378 0E2 GLU 440 14. 623 64. 277 ATOM 3187 18.346 1.00 44.99 5 ATOM 3188 C GLU 440 14. 648 17. 687 60. 854 1. 00 33. 11 61.086 1. 00 31. 25 ATOM 3189 0 GLU 440 13. 703 18. 445 ATOM 59.896 3190 N SER 441 14.613 16. 764 1. 00 34. 70 ATOM 3191 CA SER 441 13.416 16. 587 59.086 1.00 37.07 10 ATOM 3192 CBSER 441 13. 738 15. 904 57. 761 1. 00 34. 79 ATOM 3193 0G SER 441 14. 159 14. 579 57. 988 1.00 34.61 **ATOM** 3194 C SER 441 12. 452 15. 724 59. 889 1. 00 40. 43 12.866 14. 964 60.773 1. 00 38. 99 ATOM 3195 0 SER 441 ATOM 3196 N GLU 442 11. 168 15. 855 59. 571 1. 00 43. 31 ATOM 3197 CA GLU 442 10. 099 15. 135 60. 254 1. 00 45. 59 15 ATOM 3198 CBGLU 442 8. 764 15. 638 59. 724 1. 00 46. 37 ATOM 3199 CG **GLU 442** 7. 575 15. 244 60. 549 1. 00 49. 47 6.653 ATOM 3200 CD GLU 442 16. 421 60.794 1. 00 52. 25 ATOM 3201 OE1 GLU 442 5. 425 16. 199 60.895 1. 00 52. 44 ATOM 0E2 GLU 442 7. 160 17. 568 20 3202 60. 894 1. 00 53. 16 ATOM 10. 165 3203 C GLU 442 13.607 60. 174 1. 00 47. 69 ATOM 3204 0 GLU 442 10.828 13. 035 59. 314 1.00 47.21 ATOM 3205 GLU 443 9.435 12.964 61.076 N 1. 00 50. 15 ATOM 9.382 3206 CA GLU 443 11. 508 61. 210 1. 00 52. 79 8.911 ATOM 3207 CBGLU 443 11. 204 62. 623 1. 00 55. 86 25 ATOM 3208 CG GLU 443 9. 468 12. 183 63. 635 1.00 61.71 ATOM 3209 CDGLU 443 11. 962 10. 948 63. 877 1. 00 66. 19 0E1 GLU 443 ATOM 3210 11. 689 11. 746 62. 886 1. 00 68. 22 0E2 GLU 443 ATOM 3211 11. 365 12.006 65. 058 1. 00 67. 57

- 255 -8. 521 10. 711 60. 218 1. 00 53. 03 ATOM 3212 C GLU 443 **ATOM GLU 443** 7. 344 10.999 60.025 1. 00 54. 82 3213 0 ATOM 3214 N **GLY 444** 9. 116 9. 702 59. 593 1. 00 52. 26 8.861 8. 373 58. 667 1. 00 52. 32 ATOM 3215 CA GLY 444 1.00 53.07 9.389 57. 302 ATOM 3216 C **GLY 444** 7.966 5 9.460 57. 003 1. 00 52. 97 ATOM 3217 0 **GLY 444** 6. 767 1. 00 52. 71 **ATOM** 3218 N SER 445 8.961 9. 750 56. 483 8.760 10. 239 55. 104 1. 00 50. 05 ATOM 3219 CA SER 445 55. 084 ATOM 3220 CB 7.836 11. 464 1.00 51.01 SER 445 11.084 55. 318 1. 00 46. 84 ATOM 3221 OG SER 445 6. 487 10 10.076 10. 545 54. 356 1.00 46.51 ATOM 3222 C SER 445 ATOM 3223 0 SER 445 11. 123 10. 710 54. 976 1. 00 45. 30 53.026 1. 00 43. 17 3224 N 10.013 10.603 ATOM GLY 446 52. 235 11. 207 10. 842 1. 00 40. 08 ATOM 3225 CA GLY 446 11. 199 12.057 51. 330 1.00 39.05 ATOM 3226 C **GLY 446** 15 **ATOM** 3227 0 **GLY 446** 11. 414 13. 164 51. 803 1. 00 42. 74 11. 873 50. 039 1. 00 37. 60 ATOM 3228 N ARG 447 10. 940 49.098 1. 00 37. 46 ATOM 3229 CA ARG 447 10. 956 13. 000 3230 ARG 447 11. 549 12. 546 47. 747 1.00 45.51 ATOM CB 47.014 ATOM 3231 CG ARG 447 10. 793 11. 401 1. 00 53. 91 20 11. 521 10. 902 45. 743 1. 00 58. 18 ATOM 3232 CD ARG 447 NE 12. 939 10. 598 45. 975 1. 00 63. 62 ATOM 3233 ARG 447 3234 CZ ARG 447 13.399 9.623 46.769 1.00 66.02 ATOM **ATOM** 3235NH1 ARG 447 12. 560 8. 825 47. 425 1.00 67.97 NH2 ARG 447 14. 711 9. 447 46. 924 1.00 69.08 ATOM 3236 25 9. 642 13. 737 1.00 32.93 ATOM 3237 C ARG 447 48. 848 3238 0 9. 122 14. 416 49. 741 1. 00 29. 46 ATOM ARG 447 1. 00 30. 52 3239 N GLY 448 9. 150 13. 625 47.607 ATOM 1. 00 26. 03 ATOM 3240 CA GLY 448 7. 902 14. 245 47. 202

- 256 -1. 00 25. 25 **ATOM GLY 448** 6. 845 13. 828 48. 200 3241 C ATOM 3242 0 GLY 448 5. 752 14. 378 48. 244 1. 00 24. 59 1. 00 23. 74 ATOM 3243N ALA 449 7. 186 12. 840 49. 018 6. 282 12. 362 ATOM 3244 CA ALA 449 50.035 1. 00 20. 54 CB 6.611 10. 917 50.410 1. 00 18. 12 5 ATOM 3245 ALA 449 6.340 13. 251 1. 00 22. 37 ATOM 3246 C ALA 449 51. 282 3247 0 5. 307 13. 782 51.693 1.00 22.56 ATOM ALA 449 1. 00 22. 28 ATOM 3248 N ALA 450 7. 524 13. 443 51.881 ATOM 3249 CA ALA 450 7. 605 14. 261 53. 088 1. 00 20. 98 3250 CB ALA 450 9.056 14. 432 53. 535 1.00 9.63 10 ATOM **ATOM** 3251 C ALA 450 6. 937 15. 594 52. 872 1. 00 20. 66 3252 1.00 19.81 ATOM 0 ALA 450 6. 417 16. 168 53. 826 ATOM 3253 N LEU 451 6. 943 16. 109 51. 702 1. 00 19. 91 ATOM 3254 CA LEU 451 6. 279 17. 379 51.602 1. 00 22. 22 ATOM 3255 CB LEU 451 6.586 18.056 50. 279 1.00 26.74 15 3256 CG LEU 451 6. 089 19. 496 1. 00 34. 07 ATOM 50. 144 1. 00 37. 55 ATOM 3257 CD1 LEU 451 6.894 20. 425 51. 040 3258 CD2 LEU 451 6. 160 19. 955 48. 696 1. 00 36. 19 ATOM 3259 4. 774 17. 157 ATOM C LEU 451 51.686 1. 00 23. 24 4. 136 ATOM 3260 0 LEU 451 17. 474 52. 699 1. 00 21. 18 20 4. 212 ATOM 3261 N VAL 452 16. 613 50.608 1. 00 26. 44 2.798 3262 CA VAL 452 16. 405 50. 557 1. 00 26. 90 **ATOM** 3263 2. 454 15. 179 49.666 ATOM CBVAL 452 1. 00 28. 65 3. 082 ATOM 3264 CG1 VAL 452 15. 353 48. 300 1. 00 26. 01 ATOM 3265 CG2 VAL 452 2. 933 13.886 50. 313 1. 00 31. 22 25 **ATOM** 3266 C VAL 452 2. 217 16. 308 51. 935 1. 00 26. 69 **ATOM** 3267 0 VAL 452 1. 181 16.878 52. 234 1. 00 24. 86 **ATOM** 3268 N SER 453 2. 880 15. 579 52. 769 1. 00 26. 07 **ATOM** 3269 CA SER 453 2. 377 15. 346 54. 125 1. 00 26. 79

- 257 -1. 00 28. 88 3. 058 14. 127 54. 756 SER 453 ATOM 3270 CB1. 00 37. 16 SER 453 2. 553 13. 881 56. 057 **ATOM** 3271 0G 55. 028 1. 00 26. 82 SER 453 2. 571 16. 558 ATOM 3272 C 17. 301 55. 377 1. 00 26. 28 1. 658 **ATOM** SER 453 3273 0 1. 00 26. 83 16. 701 55. 389 3274 N ALA 454 3. 831 ATOM 5 1. 00 23. 37 17. 807 56. 177 4. 250 CA ALA 454 ATOM 3275 55. 937 1. 00 17. 54 5.719 18. 128 ATOM 3276 CBALA 454 1. 00 21. 80 19.002 55. 866 ALA 454 3. 381 ATOM 3277 C 19. 883 56. 714 1. 00 21. 02 3. 194 ATOM 3278 0 ALA 454 1. 00 21. 59 19.044 54. 656 2.848 ATOM 3279 N VAL 455 10 2.020 20. 156 54. 281 1. 00 25. 32 ATOM 3280 CA VAL 455 52. 841 1. 00 28. 03 2. 313 20. 557 ATOM 3281 CBVAL 455 19. 583 51. 871 1.00 29.06 1.676 ATOM 3282 CG1 VAL 455 1.00 29.98 21.961 52. 577 1.813 ATOM 3283 CG2 VAL 455 0.528 19. 890 54.469 1. 00 27. 69 C 3284 VAL 455 ATOM 15 20. 783 54. 911 1. 00 28. 10 VAL 455 -0. 202 **ATOM** 3285 0 0.061 18. 681 54. 142 1. 00 30. 51 ALA 456 ATOM 3286 N 1. 00 31. 54 -1.36718. 349 54. 318 ATOM 3287 CA ALA 456 1. 00 25. 20 -1.66616. 937 53. 836 3288 CB ALA 456 ATOM 55. 797 18. 505 1. 00 31. 77 3289 C ALA 456 -1.70220 ATOM -2. 853 18. 713 56. 176 1. 00 33. 11 ALA 456 ATOM 3290 0 1. 00 31. 33 -0.67318. 384 56. 625 N CYS 457 ATOM 3291 1. 00 33. 33 -0.84318. 538 58. 049 3292 CA CYS 457 ATOM 0. 262 17. 815 58. 811 1. 00 36. 53 3293 CB CYS 457 ATOM 1.040 16. 448 57. 890 1. 00 44. 65 CYS 457 ATOM 3294 SG 25 -0.90319.990 1. 00 34. 59 58. 438 ATOM 3295 C CYS 457 -1.74520. 391 59. 237 1. 00 34. 67 3296 CYS 457 0 ATOM 57. 881 LYS 458 0.005 20. 779 1. 00 37. 14 ATOM 3297 N 1. 00 38. 61 0.060 22. 199 58. 190 ATOM 3298 CA LYS 458

- 258 -57.669 1. 00 37. 21 **ATOM** 3299 CB LYS 458 1. 363 22. 799 LYS 458 2. 573 22. 474 58. 538 1. 00 37. 81 ATOM 3300 CG LYS 458 2. 501 23. 206 59. 874 1. 00 38. 84 ATOM 3301 CD 60. 639 1. 00 38. 18 LYS 458 3.820 23. 143 ATOM 3302 CE 24. 023 61.851 1.00 36.51 ATOM 3303 NZ LYS 458 3.812 5 22. 920 57. 596 1. 00 40. 24 C LYS 458 -1.128ATOM 3304 1. 00 39. 64 **ATOM** 3305 LYS 458 -1.37724.079 57. 898 0 -1.86922. 223 56. 752 1. 00 43. 69 **ATOM** 3306 N LYS 459 LYS 459 -3.03622. 820 56. 147 1. 00 50. 66 ATOM 3307 CA 22. 248 54. 747 1. 00 55. 88 CB LYS 459 -3.24210 ATOM 3308 -4.65722. 405 54. 183 1.00 63.64 ATOM 3309 CG LYS 459 53.856 1. 00 66. 97 ATOM 3310 CD LYS 459 -5.03723. 850 53. 226 1. 00 68. 86 CE LYS 459 -6.43123. 941 ATOM 3311 1. 00 71. 25 NZ LYS 459 -7.53123. 519 54. 152 ATOM 3312 C LYS 459 -4.26222. 562 57.018 1.00 52.41 ATOM 3313 15 23. 425 **ATOM** 3314 0 LYS 459 -5. 132 57. 132 1. 00 51. 90 -4.32221. 380 57. 634 1.00 54.96 ATOM 3315 N ALA 460 20. 997 58. 495 1. 00 57. 72 · ATOM CA ALA 460 -5. 449 3316 ATOM CB -5.20119.620 59.111 1.00 54.90 3317 ALA 460 1. 00 60. 41 **ATOM** 3318 С ALA 460 -5. 736 22. 018 59. 596 20 -6. 773 21. 950 60. 261 1. 00 60. 54 ATOM 3319 0 ALA 460 1. 00 63. 50 -4.81522. 965 59. 776 ATOM 3320 N CYS 461 3321 CA CYS 461 -4.96124. 022 60. 776 1. 00 66. 18 ATOM -3.58024. 489 1. 00 67. 98 ATOM 3322 CBCYS 461 61. 252 -3.60426. 041 62. 185 1. 00 75. 61 3323 SG CYS 461 25 ATOM -5.72725. 217 1. 00 65. 92 3324 C CYS 461 60. 200 ATOM -6.94025. 348 60.490 1. 00 65. 70 3325 0 CYS 461 **ATOM** 59. 454 1. 00 65. 20 3326 OXT CYS 461 -5.09926. 001 ATOM 7. 477 54. 655 1. 00 35. 04 ATOM 3327S S04 600 20. 241

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	ATOM	3328	01	S04	600	19. 370	7. 951	53. 566	1. 00 33. 14
	ATOM	3329	02	S04	600	20. 343	8. 532	55. 683	1. 00 32. 80
5	ATOM	3330	03	S04	600	19. 690	6. 249	55. 260	1. 00 33. 32
	ATOM	3331	04	S04	600	21. 572	7. 178	54. 108	1. 00 33. 97
	ATOM	3332	S	S04	601	22. 953	22. 471	69. 199	1. 00 77. 32
	ATOM	3333	01	S04	601	21. 971	21. 759	68. 356	1. 00 76. 19
	ATOM	3334	02	S04	601	22. 411	23. 803	69. 553	1. 00 77. 48
	ATOM	3335	03	S04	601	23. 205	21. 698	70. 433	1. 00 77. 23
	ATOM	3336	04	S04	601	24. 224	22. 628	68. 461	1. 00 77. 19
10	ATOM	3337	NA+1	NA1	602	17. 158	10. 244	54. 280	1. 00 10. 17
	ATOM	3338	OH2	НОН	603	19. 770	14. 543	47. 159	1. 00 1. 00
	ATOM	3340	0H2	НОН	604	20. 723	24. 387	67. 178	1. 00 17. 94
	ATOM	3341	0H2	НОН	605	10. 880	33. 802	37. 628	1. 00 1. 00
15	ATOM	3342	OH2	НОН	606	22. 743	28. 762	37. 147	1. 00 31. 78
	ATOM	3343	OH2	НОН	607	38. 906	1. 328	74. 611	1. 00 37. 76
	ATOM	3344	0H2	НОН	608	1. 237	30. 510	46. 162	1. 00 32. 40
	ATOM	3345	O H2	НОН	609	34. 702	-1. 731	56. 455	1. 00 62. 03
	END					•			

20 なお、表 2 は、当業者によって慣用されているプロテイン・データ・バンク の表記方法に準拠して作成されている。表 2 中、HOHは水分子を表す。

本発明においては、配列番号 5、及び/又は配列番号 8 と実質的に同一のアミノ酸配列を有し、グルコキナーゼ活性を有するタンパク質の結晶は本発明の範囲内である。そのような結晶としては、例えば、表 1、及び/又は表 2 に記載の三次元構造座標データの少なくとも一つのデータを変更した三次元構造座標データにおいて、表 1、及び/又は表 2 に記載の三次元構造座標データで示されるアミノ酸の主鎖の原子(C α 原子)と、該C α 原子と対応する前記変更した三次元構造座標データで示される C α 原子との平均二乗偏差が、0.

6 オングストローム以下である結晶が挙げられる。原子の位置を表す座標の数値が異なっても、構造座標に含まれる対応する原子の位置を重ね合わせることができる二つの構造座標は、同一の三次元構造を表すものである。

5 なお、表1、及び/又は表2に記載のGKタンパク質の三次元構造座標は、 ドラッグデザインのための重要な情報であり、必要に応じて、コンピュータ読 み取り可能な記憶媒体に保存され、コンピュータでこの情報を処理してドラッ グデザインを行う。したがって、本発明の別の態様によれば、コンピュータを、 表1、及び/又は表2に記載のアミノ酸残基の三次元座標を記憶する三次元座 標記憶手段として機能させるためのプログラムを記録したコンピュータ読み取 り可能な記録媒体が提供される。

また、本発明の別の態様によれば、コンピュータを、表1、及び/又は表2 に記載のアミノ酸残基の三次元座標に関する情報を記憶した三次元座標記憶手 段と、前記三次元座標記憶手段に記憶された表1、及び/又は表2に記載のア ミノ酸残基の三次元座標を用いて配列番号5、及び/又は配列番号8で表され 15 るアミノ酸配列を有するタンパク質の化合物結合部位を推測する結合部位推測 手段と、タンパク質と結合する化合物の種類と、当該化合物の三次元構造に関 する情報を記憶した結合化合物記憶手段と、少なくとも、前記結合部位推測手 段によって推測された配列番号5、及び/又は配列番号8で表されるアミノ酸 配列を有するタンパク質の化合物結合部位の三次元構造に関する情報と、前記 20 結合化合物記憶手段に記憶された化合物の三次元構造に関する情報とを用いて 前記配列表の配列番号1で表されるアミノ酸配列を有するタンパク質の化合物 結合部位に適合する化合物の候補を選択する結合化合物候補選択手段、として 機能させるプログラムを記録したコンピュータ読み取り可能な記録媒体が提供 される。さらに、本発明の別の態様によれば、上記各手段を備えるコンピュー 25 夕も提供される。

(GKタンパク質とそれに結合する化合物との複合体の結晶) 次に、本発明の別の態様によれば、配列番号5、又は配列番号8に記載のア ミノ酸配列又はそのアミノ酸配列と実質的に同一のアミノ酸配列を含むタンパク質と該タンパク質に結合可能な化合物との複合体を含む結晶及びその製造方法が提供される。

GKタンパク質と結合する化合物が得られた場合は、まず、GKタンパク質とその化合物を、例えば、水溶液中で混合し、複合体を形成する。このような複合体の結晶は、共結晶法、ソーキング法などの公知の共結晶の製造方法が用いられる。結晶化条件、結晶化方法については、上述した方法が参照される。

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GKタンパク質と結合する化合物は、例えば、上記式(I)で表される化合物群から選択される。

10 ここで、上記式(I)のハロゲン原子としては、フッ素原子、塩素原子、臭素原子、ヨウ素原子などが例示され、これらの中でも塩素原子が好ましい。

また、上記式(I)のA、B及び式(I I)のヘテロアリール基における置換基としては、アミノ基、カルバモイル基、カルバモイルアミノ基、カルバモイルオキシ基、カルボキシル基、シアノ基、スルファモイル基、トリフルオロメチル基、ハロゲン原子、ヒドロキシ基、ホルミル基、直鎖の C_1-C_6 アルキル基、環状の C_3-C_6 炭化水素基、アラルキル基、N-アラルキルアミノ基、

N, N-ジアラルキルアミノ基、アラルキルオキシ基、アラルキルカルボニル 基、N-アラルキルカルバモイル基、アリール基、アリールチオ基、N-アリ ールアミノ基、アリールオキシ基、アリールスルホニル基、アリールスルホニ

20 ルオキシ基、N-アリールスルホニルアミノ基、アリールスルファモイル基、N-アリールカルバモイル基、アロイル基、アロキシ基、 C_2- C $_6$ アルカノイル基、N-C $_2-$ C $_6$ アルカノイルアミノ基、 C_1- C $_6$ アルキルチオ基、N-C $_1-$ C $_6$ アルキルスルファモイル基、N, N-ジー C_1- C $_6$ アルキルスルファモイル基、N, N-ジーN0.

N- C_1 - C_6 アルキルスルホニルアミノ基、 C_1 - C_6 アルコキシ基、 C_1 - C_6 アルコキシカルボニル基又は C_1 - C_6 アルキルアミノ基を示す)などが挙げられる。ここで用いられる好ましい置換基は、アミノ基、カルバモイル基、カルバモイルアミノ基、カルバモイルオキシ基、カルボキシル基、シアノ基、スルファモイル基、トリフルオロメチル基、ハロゲン原子、ヒドロキシ基、ホルミ

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ル基、直鎖のC₁-C₆アルキル基などが例示される。

ここで、「炭化水素基」は、炭素数1乃至6の直鎖のアルキル基を示すか、 又は該アルキル基を構成する炭素原子のうち、1又は2の、好ましくは1の炭 素原子が窒素原子、硫黄原子又は酸素原子で置き換わっていてもよいか、及び /又は該炭素数1乃至6の直鎖のアルキル基中の炭素原子同士が二重結合又は 三重結合で結合されていてもよい基である。該二重結合又は三重結合の数は、 1又は2であることが好ましく、1であることがより好ましい。

該炭化水素基としては、具体的には、メチル基、エチル基、プロピル基若しくはイソプロピル基、ブチル基又は下記式

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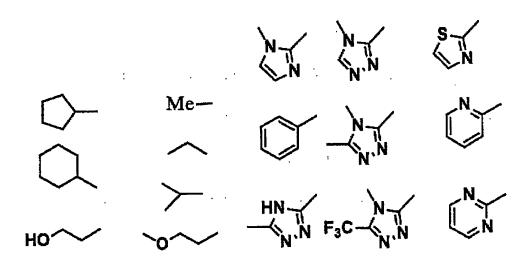
で表される基であることが好ましい。より好ましい炭化水素基は、メチル基、 エチル基、プロピル基、イソプロピル基又は下記式

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で表される基である。

好ましいAとしては(p=0の場合)、例えば、次の基が挙げられる。

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好ましいBとしては、例えば、次の基が挙げられる。

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式(II)で示されるヘテロアリール基としては、例えば、次の複素環基が 5 挙げられる。

なお、特に好ましい化合物は、上述した式(IIIa) ~式(IIIc) で表される いずれかの化合物である。

本発明の化合物(I)は、公知の反応手段を用いるか、或いは公知の方法に従って容易に製造することができる。なお、本発明の一般式(I)の化合物は、通常の液相における合成のみならず、近年発達の目覚しい例えばコンビナトリアル合成法やパラレル合成法等の固相を用いた合成によっても製造することができる。好ましくは例えば以下の方法により製造することができる。

PCT/JP03/06054 WO 03/097824

[式中、各記号は前記定義に同じ]

(工程1)

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本工程は、カルボン酸化合物(1)又はその反応性誘導体と前記式(2)で 表される置換されていてもよい単環の、又は双環のヘテロアリール基を有する アミノ化合物又はその塩とを反応させて、化合物(3)を製造する方法である。 本反応は文献記載の方法(例えば、ペプチド合成の基礎と実験、泉屋信夫他、 丸善、1983年、コンプリヘンシブ オーガニック シンセシス (Comp rehensive Organic Synthesis)、第6巻、Pe 10 rgamon Press社、1991年、等)、それに準じた方法又はこれ らと常法とを組み合わせることにより、通常のアミド形成反応を行えばよく、 即ち、当業者に周知の縮合剤を用いて行うか、或いは、当業者に利用可能なエ ステル活性化方法、混合酸無水物法、酸クロリド法、カルボジイミド法等によ り行うことができる。このようなアミド形成試薬としては、例えば塩化チオニ 15 ル、N, N-ジシクロヘキシルカルボジイミド、1-メチル-2-ブロモピリ ジニウムアイオダイド、N, N'-カルボニルジイミダゾール、ジフェニルフ ォスフォリルクロリド、ジフェニルフォスフォリルアジド、N, N'ージスク

シニミジルカルボネート、 N, N'ージスクシニミジルオキザレート、1ーエチルー3ー(3ージメチルアミノプロピル)カルボジイミド塩酸塩、クロロギ酸エチル、クロロギ酸イソブチル又はベンゾトリアゾー1ーリルーオキシートリス(ジメチルアミノ)フォスフォニウムへキサフルオロフォスフェイト等が挙げられ、中でも例えば塩化チオニル、N, Nージシクロヘキシルカルボジイミド又はベンゾトリアゾー1ーリルーオキシートリス(ジメチルアミノ)フォスフォニウムヘキサフルオロフォスフェイト等が好適である。またアミド形成反応においては、上記アミド形成試薬と共に塩基、縮合補助剤を用いてもよい。

用いられる塩基としては、例えばトリメチルアミン、トリエチルアミン、N, Nージイソプロピルエチルアミン、Nーメチルモルホリン、Nーメチルピロリジン、Nーメチルピペリジン、N, Nージメチルアニリン、1, 8ージアザビシクロ[5.4.0]ウンデカー7ーエン(DBU)、1, 5ーアザビシクロ[4.3.0]ノナー5ーエン(DBN)等の第3級脂肪族アミン;例えばピリジン、4ージメチルアミノピリジン、ピコリン、ルチジン、キノリン又はイソキノリン等の芳香族アミン等が挙げられ、中でも例えば第3級脂肪族アミン等が好ましく、特に例えばトリエチルアミン又はN, Nージイソプロピルエチルアミン等が好適である。

用いられる縮合補助剤としては、例えばN-ヒドロキシベンゾトリアゾール水和物、N-ヒドロキシスクシンイミド、N-ヒドロキシ-5-ノルボルネン-2,3-ジカルボキシイミド又は3-ヒドロキシ-3,4-ジヒドロ-4-オキソ-1,2,3-ベンゾトリアゾール等が挙げられ、中でも例えばN-ヒドロキシベンゾトリアゾール等が好適である。

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用いられるアミノ化合物(2)の量は、用いられる化合物及び溶媒の種類その他の反応条件により異なるが、通常カルボン酸化合物(1)又はその反応性誘導体1当量に対して、0.02乃至50当量、好ましくは0.2乃至2当量である。ここにおいて、反応性誘導体としては、通常有機化学の分野において用いられる、例えば活性エステル誘導体、活性アミド誘導体等が挙げられる。

用いられるアミド形成試薬の量は、用いられる化合物及び溶媒の種類その他

の反応条件により異なるが、通常カルボン酸化合物(1)又はその反応性誘導体1当量に対して、1乃至50当量、好ましくは1乃至5当量である。

用いられる縮合補助剤の量は、用いられる化合物及び溶媒の種類その他の反応条件により異なるが、通常カルボン酸化合物(1)又はその反応性誘導体1 当量に対して、1乃至50当量、好ましくは1乃至5当量である。

用いられる塩基の量は、用いられる化合物及び溶媒の種類その他の反応条件 により異なるが、通常1万至50当量、好ましくは3万至5当量である。

本工程において用いられる反応溶媒としては、例えば不活性有機溶媒であり、反応に支障のない限り、特に限定されないが、具体的には、例えば塩化メチレン、クロロホルム、1,2ージクロロエタン、トリクロロエタン、N,Nージメチルホルムアミド、酢酸エチルエステル、酢酸メチルエステル、アセトニトリル、ベンゼン、キシレン、トルエン、1,4ージオキサン、テトラヒドロフラン、ジメトキシエタン又はそれらの混合溶媒が挙げられるが、好適な反応温度確保の点から、特に例えば塩化メチレン、クロロホルム、1,2ージクロロエタン、アセトニトリル又はN,Nージメチルホルムアミド等が好適である。

反応温度は、-100℃乃至溶媒の沸点温度、好ましくは0乃至30℃である。

反応時間は、0.5乃至96時間、好ましくは3乃至24時間である。

本工程1で用いられる塩基、アミド形成試薬、縮合補助剤は、一種又はそれ 20 以上組み合わせて使用することができる。

化合物(3)が保護基を有している場合には、適宜当該保護基を除去することが可能である。当該補助基の除去は、文献記載の方法(プロテクティブ グループス イン オーガニック シンセシス(Protective Groupsin Organic Synthesis)、T. W. Green著、第2版、<math>John Wiley & Sons社、1991年、等)、それに準じた方法又はこれらと常法とを組み合わせることにより行うことができる。

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このようにして得られる化合物(3)は、公知の分離精製手段、例えば濃縮、減圧濃縮、結晶化、溶媒抽出、再沈殿、クロマトグラフィー等により単離精製するか又は単離精製することなく次工程に付すことができる。

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(工程2)

本工程は、上記工程1で得られたアミド化合物(3)と化合物(4)とを反応させることにより化合物(5)を製造する方法である。

本反応においては、反応系中に必要に応じて塩基を加えてもよい。用いられ 5 る化合物(4)としては、好ましくはフェノール誘導体又はチオール誘導体が 好ましい。該フェノール誘導体又はチオール誘導体としては、例えばフェノー ル、チオフェノール、チオイミダゾール、チオトリアゾール等が挙げられる。 用いられる化合物(4)の量は、用いられる化合物及び溶媒の種類その他の反 応条件により異なるが、通常アミノ誘導体(3)1当量に対して、2乃至50 10 当量、好ましくは2乃至5当量である。用いられる塩基としては、例えばトリ メチルアミン、トリエチルアミン、N. N – ジイソプロピルエチルアミン、N ーメチルモルホリン、N-メチルピロリジン、N-メチルピペリジン、N,N ージメチルアニリン、1、8ージアザビシクロ[5.4.0]ウンデカー7ー エン (DBU)、1,5-アザビシクロ[4.3.0]ノナー5-エン (DB 15 N) 等の第3級脂肪族アミン:例えばピリジン、4-ジメチルアミノピリジン、 ピコリン、ルチジン、キノリン又はイソキノリン等の芳香族アミン;例えば金 属カリウム、金属ナトリウム、金属リチウム等のアルカリ金属;例えば水素化 ナトリウム、水素化カリウム等のアルカリ金属水素化物;例えばプチルリチウ ム等のアルカリ金属アルキル化物;例えばカリウムーtertーブチラート、 20 ナトリウムエチラート又はナトリウムメチラート等のアルカリ金属アルコキシ ド:例えば水酸化カリウム、水酸化ナトリウム等のアルカリ金属水酸化物;例 えば炭酸カリウム等のアルカリ金属炭酸塩等が挙げられ、中でも例えば第3級 脂肪族アミン、アルカリ金属水素化物又はアルカリ金属炭酸塩が好ましく、特 に例えばトリエチルアミン、N, N-ジイソプロピルエチルアミン、水素化ナ 25 トリウム又は炭酸カリウムが好適である。

用いられる当該塩基の量は、用いられる化合物及び溶媒の種類その他の反応 条件により異なるが、アミド化合物(3)1当量に対して通常0乃至50当量、 好ましくは2乃至10当量である。該塩基は、必要に応じて一種又は2種以上

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用いることができる。

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用いられる不活性有機溶媒としては、反応に支障のないものであれば、特に限定されないが、具体的には、例えば塩化メチレン、クロロホルム、1,2-ジクロロエタン、トリクロロエタン、N,N-ジメチルホルムアミド、N,N-ジメチルアセトアミド、酢酸エチルエステル、酢酸メチルエステル、アセトニトリル、ベンゼン、キシレン、水、トルエン、1,4-ジオキサン、テトラヒドロフラン又はこれらの混合溶媒等が挙げられる。

このようにして得られる化合物(5)は、公知の分離精製手段、例えば濃縮、減圧濃縮、結晶化、溶媒抽出、再沈殿、クロマトグラフィー等により単離精製 することができる。

(工程3)

本工程は化合物(5)を還元して、本発明で用いる化合物(I)を製造する方法である。本工程において用いられる還元反応は、当業者に周知の方法が用いられる。本工程においてもちいられる還元反応としては、具体的には、例えば(1)水素、蟻酸、蟻酸アンモニウム、ヒドラジン水和物とパラジウム、白金、ニッケル触媒を用いる接触還元法、(2)塩酸、塩化アンモニウムと鉄を用いる還元法、(3)メタノールと塩化スズを用いる還元法等が挙げられる。

上記還元反応において用いられる還元剤の量は、用いられる化合物及び溶媒 20 の種類その他の反応条件により異なるが、化合物(5)1当量に対して通常1 乃至50当量、好ましくは2乃至20当量である。

用いられる反応溶媒としては、反応に支障のない限り、特に限定されないが、例えばジクロロメタン、クロロホルム等のハロゲン化炭化水素類、例えばジエチルエーテル、tertーブチルメチルエーテル、テトラヒドロフラン等のエーテル類、例えばN,Nージメチルホルムアミド、N,Nージメチルアセトアミド等のアミド類、例えばジメチルスルホキシド等のスルホキシド類、例えばアセトニトリル等のニトリル類、例えばメタノール、エタノール、プロパノール等のアルコール類、例えばベンゼン、トルエン、キシレン等の芳香族炭化水素類、水或いはこれらの混合溶媒を用いることができる。

反応温度及び反応時間は特に限定されないが、-10乃至1.00℃程度、好ましくは0乃至50℃程度の反応温度で1乃至20時間程度、好ましくは1乃至5時間程度反応を行う。

このようにして得られる本発明で用いる化合物(I)は、公知の分離精製手 5 段、例えば濃縮、減圧濃縮、結晶化、溶媒抽出、再沈殿、クロマトグラフィー 等により単離精製するか又は単離精製することなく、次工程に付すことができ る。

上記各工程の化合物は、各置換基上に保護基を有していてもよい。当該保護基は、各工程において適宜、公知の方法これに準じた方法、又はこれらと常法とを組み合わせた方法により除去することができる。除去の態様は、化合物、反応の種類その他の反応条件により、適宜の除去反応が可能であるが、個別に各保護基を除去する場合、各保護基を同時に除去する場合等が考えられ、当業者が適宜選択可能である。当該保護基としては、例えばヒドロキシ基の保護基、アミノ基の保護基、カルボキシル基の保護基、アルデヒドの保護基、ケト基の保護基等が挙げられる。また、当該保護基の除去順序は、特に限定されるものではない。

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ヒドロキシ基の保護基としては、例えばtertーブチルジメチルシリル基、 tertーブチルジフェニルシリル基等の低級アルキルシリル基、例えばメト キシメチル基、2-メトキシエトキシメチル基等の低級アルコキシメチル基、 例えばベンジル基、p-メトキシベンジル基等のアラルキル基、例えばホルミ ル基、アセチル基等のアシル基等が挙げられ、これらのうち、特にtertー ブチルジメチルシリル基、アセチル基等が好ましい。

アミノ基の保護基としては、例えばベンジル基、p-ニトロベンジル基等のアラルキル基、例えばホルミル基、アセチル基等のアシル基、例えばエトキシカルボニル基、tertーブトキシカルボニル基等の低級アルコキシカルボニル基、例えばベンジルオキシカルボニル基、p-ニトロベンジルオキシカルボニル基等のアラルキルオキシカルボニル基等が挙げられ、これらのうち、特にニトロベンジル基、tertーブトキシカルボニル基、ベンジルオキシカルボニル基等が好ましい。

カルボキシル基の保護基としては、例えばメチル基、エチル基、tertーブチル基等の低級アルキル基、例えばベンジル基、p-メトキシベンジル基等のアラルキル基等が挙げられ、これらのうち、特にメチル基、エチル基、tertーブチル基、ベンジル基等が好ましい。

5 ケト基の保護基としては、例えばジメチルケタール基、1,3-ジオキシラン基、1,3-ジオキソラン基、1,3-ジチアン基、1,3-ジチオラン基等が挙げられ、これらのうち、ジメチルケタール基、1,3-ジオキソラン基等がより好ましい。

アルデヒド基の保護基としては、例えば、ジメチルアセタール基、1,3-10 ジオキシラン基、1,3-ジオキソラン基、1,3-ジチアン基、1,3-ジチアン基、1,3-ジオチオラン基等が挙げられ、これらのうちジメチルアセタール基、1,3-ジオキソラン基等がより好ましい。

本発明で用いる化合物を製造するに当たっては、反応を効率よく進行させるために、官能基に保護基を導入する場合もある。これらの保護基の導入は、当 業者に適宜選択可能であり、当該保護基の除去は、前記記載のプロテクティブグループス イン オーガニックシンセシス等の方法、これに準じた方法又はこれらと常法とを組み合わせることにより行うことができる。なお、保護基の除去の順序についても、当業者が適宜選択可能である。

このようにして得られる化合物 (I) は、公知の分離精製手段、例えば濃縮、 20 減圧濃縮、結晶化、再沈殿、溶媒抽出、クロマトグラフィー等により単離精製 するか又は単離精製することなく次工程に付すことができる。

また、本発明で用いる化合物である(I)は、下記の工程によっても製造することができる。

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[式中各記号は前記定義に同じ]

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上記工程4、工程5及び工程6については、試薬の量、反応溶媒、反応温度 5 等その他の反応条件は、前記工程2、工程1及び工程3と同様にして行うこと ができる。

R²に保護基が必要な場合には、前記記載のプロテクティブグループス イ ンオーガニックシンセシス等の方法、それに準じた方法又はこれらと常法とを 組み合わせることにより、当業者が保護基を適宜選択することによって行うこ とができる。

このようにして得られる化合物(6)、(5')は、公知の分離精製手段、 例えば濃縮、減圧濃縮、結晶化、再沈殿、溶媒抽出等により単離精製するか、 又は単離精製することなく次工程に付すことができる。

本発明で用いる化合物(I)は、公知の分離精製手段、例えば濃縮、減圧濃 縮、結晶化、再沈殿、溶媒抽出等により単離精製することができる。 15

上記工程1乃至6において、保護基の除去は、当該保護基の種類及び化合物 の安定性により異なるが、前記記載のプロテクティブ グループス イン オ ーガニック シンセシス ((Protective Groups in O

rganic Synthesis)、T.W.Green著 第2版、John Wiley&Sons社、1991年、等)、それに準じた方法又はこれらと常法とを組み合わせることにより行うことができる。例えば酸又は塩基を用いる加溶媒分解、水素化金属錯体等を用いる化学的還元又はパラジウム炭素触媒、ラネーニッケル等を用いる接触還元等により行うことができる。

本発明によって提供されるベンズアミド化合物は、薬学的に許容される塩として存在することができる。当該塩は、常法に従って製造することができる。 具体的には、上記化合物(I)が、当該分子内に例えばアミノ基、ピリジル基等に由来する塩基性基を有している場合には、当該化合物を酸で処理することにより、相当する薬学的に許容される塩に変換することができる。

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当該酸付加塩としては、例えば塩酸塩、フッ化水素酸塩、臭化水素酸塩、ヨウ化水素酸塩等のハロゲン化水素酸塩;硝酸塩、過塩素酸塩、硫酸塩、燐酸塩、炭酸塩等の無機酸塩;メタンスルホン酸塩、トリフルオロメタンスルホン酸塩、エタンスルホン酸塩等の低級アルキルスルホン酸塩;ベンゼンスルホン酸塩、

15 p-トルエンスルホン酸塩等のアリールスルホン酸塩;フマル酸塩、コハク酸塩、クエン酸塩、酒石酸塩、シュウ酸塩、マレイン酸塩等の有機酸塩;及びグルタミン酸塩、アスパラギン酸塩等のアミノ酸等の有機酸である酸付加塩を挙げることができる。また、本発明の化合物が酸性基を当該基内に有している場合、例えばカルボキシル基等を有している場合には、当該化合物を塩基で処理することによっても、相当する薬学的に許容される塩に変換することができる。当該塩基付加塩としては、例えば例えばナトリウム、カリウム等のアルカリ金属塩、カルシウム、マグネシウム等のアルカリ土類金属塩、アンモニウム塩、グアニジン、トリエチルアミン、ジシクロヘキシルアミン等の有機塩基による塩が挙げられる。さらに本発明の化合物は、遊離化合物又はその塩の任意の水和りは溶媒和物として存在してもよい。

本発明においては、実施例の記載にて詳述するように、配列番号5に示すアミノ酸配列を有するGKタンパク質と上記式(IIIa)~式(IIIc)との化合物の複合体の結晶が得られている。これらの、結晶の3次元構造座標を解析することによって、配列番号5で示すGKタンパク質においては、化合物結合部位

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が、チロシン61~セリン69、グルタミン酸96~グルタミン98、イソロイシン159、メチオニン210~チロシン215、ヒスチジン218~グルタミン酸221、メチオニン235、アルギニン250、ロイシン451~リジン459のアミノ酸残基から構成されることが解明されている。

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なお、本発明の別の態様によれば、配列番号2に記載のアミノ酸配列を有するタンパク質から、上述のようにN末端側、および/またはC末端側の所定の数のアミノ酸残基を欠損したアミノ酸配列を有するタンパク質を製造するタンパク質製造工程と、前記タンパク質製造工程で得られたタンパク質と結合する化合物と、前記タンパク質製造工程で得られたタンパク質とを反応させる工程とを含む、タンパク質及びそのタンパク質と結合する化合物の複合体を含む結晶を製造する方法が提供される。

上記タンパク質製造工程において製造されるタンパク質としては、結晶内で 隣接するGKタンパク質との間で立体的な障害がなくなる範囲であればその数 は限定されない。具体的には、例えば、配列番号 2 で表されるアミノ酸配列において、N 末端側の $1\sim5$ 0個、好ましくは $3\sim3$ 0個、より好ましくは $5\sim2$ 5個、さらに好ましくは $8\sim1$ 8個、特に好ましくは $11\sim1$ 5個のアミノ酸残基を欠失させたアミノ酸配列などが挙げられる。また、C 末端側の $1\sim8$ 個、好ましくは $1\sim7$ 個、より好ましくは $2\sim6$ 個のアミノ酸残基を欠失させたアミノ酸配列などが挙げられる。

(3次元構造座標を用いるドラッグデザイン方法)

上記のようにして得られる本発明のGKタンパク質の3次元構造は、CAR DD (Computer Aided Rational Drug Design)による創薬システムのための重要な情報である。このGKタンパク質の活性中心、及びアロステリック部位を明らかにし、その部位に適合し、GKタンパク質と相互作用することにより、GKタンパク質を阻害、または活性化する物質を検索することは、GKタンパク質をターゲットとする創薬開発の重要なステップである。

すなわち、本発明の別の態様によれば、タンパク質の立体構造情報に基づい

て該タンパク質に結合する化合物の構造をデザインするドラッグデザイン方法であって、該タンパク質の立体構造情報が、上述のようにして得られる結晶を解析することによって得られる情報であることを特徴とする、ドラッグデザイン方法が提供される。このようなドラッグデザイン方法としては、エネルギー計算、若しくはこれに類似する活性予測値、又はファルマコフォアを用いてドラッグデザインする手法と、コンピュータグラフィックスの技術を用いて視覚的にドラッグデザインをする手法がある。

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エネルギー計算、若しくはこれに類する活性予測値、又はファルマコフォアを用いる手法による方法としては、(1)上述したようにして得られる立体構造情報に基づいて、上記タンパク質の化合物結合部位を推測する結合部位推測工程と、前記結合部位推測工程で推測された化合物結合部位に適合する化合物を、化合物ライブラリより選択する選択工程とを含むことを特徴とするドラッグデザイン方法、(2)前記立体構造情報に基づいて、前記タンパク質の化合物結合部位を推測する結合部位推測工程と、前記結合部位推測工程で推測された化合物結合部位に適合する化合物の構造を構築する化合物構造構築工程とを含むことを特徴とする、ドラッグデザイン方法などが例示される。

上記タンパク質の化合物結合部位を推測する方法としては、例えば、化合物との共結晶においてリガンドが結合している部位をコンピュータのディスプレイ上で目視で確認して特定する方法の他、リガンドが結合していない状態で解かれたタンパク質結晶構造に対してリガンドが結合しそうな部位を推定して特定する方法が挙げられる。いずれの方法においても公知の方法や市販のコンピュータソフトウエアを用いることができる。前者の方法においては、例えば、Insight II (Accelrys Inc.)、SYBYL (Tripos Inc.)、MOE (Chemical Computing Group)等のソフトウエアを用いることができる。一方、後者の方法においては、例えば、Cavity search: an algorithm for the isolation and display of cavity-like binding regions. (Journal of Computer-Aided Molecular Design. 4(4):337-54, 1990)等の公知の手法を用いることができ、SiteID (Tripos Inc.)等のソフトウエアを用いて実施することができる。

タンパク質における化合物との結合部位が推測できたら、その推測された結

合部位に適合し得る化合物を選択する。この化合物候補を選択する方法としては、既存の化合物ライブラリからの化合物の構造情報を入手して、そのライブラリ中の化合物の構造情報と上記のようにして推測された結合部位の構造情報とを比較することによって、結合可能化合物候補を選択する。

5 より具体的には、配列番号 5 に示すアミノ酸配列のアミノ酸残基(チロシン 61~セリン 69、グルタミン酸 96~グルタミン 98、イソロイシン 159、メチオ ニン 210~チロシン 215、ヒスチジン 218~グルタミン酸 221、メチオニン 235、アルギニン 250、ロイシン 4 5 1~リジン 4 5 9)から1つないしは2つ以上 の残基もしくは複合体中のリガンドの官能基から形成される水素結合性または 10 疎水性などのファルマコフォアと、蛋白構造またはその一部の側鎖の配向を改変させた構造から作成される蛋白表面を検索条件として、化合物ライブラリより各化合物の配座、配向を網羅的に探索しながら条件を満たすかどうかを判断して選択する。

他の代替方法として、化合物ライブラリより各化合物の配座、配向を網羅的に探索しながら、アミノ酸残基(チロシン 61~セリン 69、グルタミン酸 96~グルタミン 98、イソロイシン 159、メチオニン 210~チロシン 215、ヒスチジン 218~グルタミン酸 221、メチオニン 235、アルギニン 250、ロイシン 451~リジン 459)から構成されるリガンド結合部位の構造またはその一部の側鎖の配向を改変させた構造に対して候補化合物をバーチャルでドッキングさせ、アミノ酸残基(チロシン 61~セリン 69、グルタミン酸 96~グルタミン 98、イソロイシン 159、メチオニン 210~チロシン 215、ヒスチジン 218~グルタミン酸 221、メチオニン 235、アルギニン 250、ロイシン 451~リジン 459)から1つないしは2つ以上の残基と 4オングストローム以下で近接した相互作用を形成したものを選択したり、エネルギー評価関数を用いた選択を行う。

25 一方、候補化合物は、上記のようにして推測された結合部位の構造情報に基づいて結合可能化合物を設計することによっても選択することができる。より 具体的には、配列番号 5 に示すアミノ酸配列のアミノ酸残基 (チロシン 61~セリン 69、グルタミン酸 96~グルタミン 98、イソロイシン 159、メチオニン 210~チロシン 215、ヒスチジン 218~グルタミン酸 221、メチオニン 235、ア

ルギニン 250、ロイシン 4 5 1 ~ リジン 4 5 9)から構成される化合物結合部位の構造またはその一部の側鎖の配向を改変させた構造に対して、1つないしは2つ以上の残基と相互作用するように各種原子種、官能基を種々つなぎ合わせて化合物構造を構築する。この方法としては、メチル、エチル等の化学基を活性部位に並べて適合する化合物を探す方法と、原子を活性部位にコンピュータプログラムを用いて結合させていく方法とが知られている。

なお、コンピュータによるエネルギー評価による方法では、例えば分子力場 計算を用いて化合物と、GKタンパク質との結合のエネルギーを求める方法が 挙げられる。その計算をデータベースの中の各化合物に適用し、安定に結合で きる化合物候補を、ライブラリ化合物の中から求める。Insight II のLudiなどコンピュータプログラムによっては、蛋白質分子において相互 作用するアミノ酸残基の3次元構造座標を与えると、自動的に結合可能な化合 物の候補を選択し出力するものもあり、好適に利用することができる。

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また、分子の3次元構造に基づくドラッグデザインについては、医薬品の開発・第7巻「分子設計」(廣川書店)をはじめとして数多くの文献が知られている。具体的には、第一にFlexiDock、FlexX等のフレキシブルリガンドバインディングシミュレーションソフトウエアを用いて、低分子(分子量1000以下)化合物のライブラリ(たとえば約150000種)をコンピュータでスクリーニングすることができる。このライブラリ内の化学物質はCONCORD等のプログラムで3次元構造を構築し、活性部位に適合する化合物を選択することができる。

一方、目視的によりドラッグデザインする方法としては、前記立体構造情報に基づいて、前記タンパク質の化合物結合部位を推測する結合部位推測工程と、前記結合部位推測工程で推測された化合物結合部位と該化合物結合部位に適合する化合物とが相互作用するように化合物の構造を目視によりデザインするデザイン工程とを含むことを特徴とする、ドラッグデザイン方法が挙げられる。例えば、配列番号 5 に示すアミノ酸配列のアミノ酸残基(チロシン 61~セリン 69、グルタミン酸 96~グルタミン 98、イソロイシン 159、メチオニン 210~チロシン 215、ヒスチジン 218~グルタミン酸 221、メチオニン 235、アルギ

ニン 250、ロイシン4 5 1 ~ リジン4 5 9)から構成されるリガンド結合部位 の構造またはその一部の側鎖の配向を改変させた構造に対して、これらの残基 のうち 1 つないしは 2 つ以上の残基と相互作用するように目視による構造構築、もしくは構造改変を行う。

具体的には、視覚的方法では、まずコンピュータの画面上にGKタンパク質 5 とそれに結合する化合物との複合体の結晶の構造を、得られた構造座標に従っ て表示する。そして、コンピュータ上で化学的相互作用を考慮しながら、ライ ブラリ中にある化合物とGKタンパク質との結合可能性を順次検討する。ここ で考慮すべき化学的相互作用は静電相互作用、疎水性相互作用、水素結合、フ ァンデルワールス相互作用などである。すなわち、該化合物の3次元空間での 10 構造が、その官能基群においてカルボキシル基、ニトロ基、ハロゲン基などの 陰性電荷を帯びやすい基が、GKタンパク質のリジン、アルギニン、ヒスチジ ンといった正電荷を持つアミノ酸残基に相互作用するように、アミノ基、イミ ノ基、グアニジル基などの陽性電荷を帯びやすい基が、GKタンパク質のグル タミン酸、アスパラギン酸といった負電荷を持つアミノ酸残基に相互作用する ように、脂肪族基や芳香族基といった疎水性の官能基が、アラニン、ロイシン、 イソロイシン、バリン、プロリン、フェニルアラニン、トリプトファン及びメ チオニンといった疎水性のアミノ酸残基と相互作用するように、水酸基、アミ ド基などの水素結合に関与する基が、GKタンパク質の主鎖や側鎖部分と水素 結合ができるように、更には、該化合物とGKタンパク質の結合において立体 20 的な障害が生じないように、また、更には、空隙部分がなるべくできないよう に空隙部分が充填され、ファンデルワールス相互作用が大きくなるようになど、 相互作用に好ましい構造になっているかを総合的に考慮する。このように、静 電相互作用、疎水性相互作用、ファンデルワールス相互作用、水素結合などの 因子を、コンピュータ画面上で視覚的に総合的に考慮して、最終的に候補化合 25 物がGKタンパク質に結合し得るか否かの判断を行う。

このように目視によって化合物候補を選択するプログラムとしては、 Insight II や MOE 等のシミュレーションプログラムが例示される。 G K タン パク質と相互作用する化合物の有力候補を挙げるために、 候補化合物と G K タ

ンパク質と接触させ、GKタンパク質の活性を測定する。有力候補化合物を実際にGKタンパク質と混合し、結晶化し適合するかどうかを検討する。更に適合した複合物を有機合成を用いて修飾することにより、より望ましい構造とする

- 5 なお、視覚的手法と、エネルギーを考慮した手法は、適宜組合わせて用いることもできる。そのようなコンピュータソフトウエアとしては、FlexiDock (Tripos Inc.)、FlexX (Tripos Inc.)、SYBYL (Tripos Inc.)、Insight II (Accelrys Inc.)、MOE (Chemical Computing Group Inc.) などが挙げられる。
- なお、本発明においては、上述したドラッグデザイン方法によって選択された化合物を実際に合成し、これらの化合物群を化合物アレイ(又は化合物ライブラリ)として提供することができる。このような化合物アレイを利用すれば、ハイスループットスクリーニングの技術などを用いて、一度に大量の候補化合物をアッセイすることができるので、グルコキナーゼの活性化剤又は阻害剤を効率良くスクリーニングすることができる。

(本発明の方法によって得られる化合物及びそれを含む治療剤)

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上記のドラッグデザイン方法によって設計される化合物は、グルコキナーゼと結合する能力を有するので、グルコキナーゼの活性化化合物又はグルコキナーゼ阻害化合物として用いることができる。また、このような化合物を含有する治療剤又は医薬組成物は、グルコキナーゼ活性が関与する疾患の治療剤(例えば、糖尿病治療剤)として有効に用いることができる。

上記医薬組成物は、本発明のグルコキナーゼと結合する化合物を有効成分として、その薬学的有効量を、適当な薬学的に許容される担体ないし希釈剤と共に含有する。上記医薬組成物(医薬製剤)に利用できる薬学的に許容できる担体としては、製剤の使用形態に応じて通常使用される、充填剤、増量剤、結合剤、付湿剤、崩壊剤、表面活性剤、滑沢剤などの希釈剤或は賦形剤などが例示される。これらの担体は、得られる製剤の投与単位形態に応じて適宜選択使用される。

本発明の医薬組成物の投与単位形態としては、各種の形態が治療目的に応じ て選択でき、その代表的なものとしては、錠剤、丸剤、散剤、粉末剤、顆粒剤、 カプセル剤などの固体投与形態や、溶液、懸濁剤、乳剤、シロップ、エリキシ ルなどの液剤投与形態が含まれ、これらは更に投与経路に応じて経口剤、非経 口剤、経鼻剤、経膣剤、坐剤、舌下剤、軟膏剤などに分類され、それぞれ通常 の方法に従い、調合、成形、調製することができる。例えば、錠剤の形態に成 形するに際しては、上記製剤担体として例えば乳糖、白糖、塩化ナトリウム、 ブドウ糖、尿素、デンプン、炭酸カルシウム、カオリン、結晶セルロース、ケ イ酸、リン酸カリウムなどの賦形剤、水、エタノール、プロパノール、単シロ ップ、ブドウ糖液、デンプン液、ゼラチン溶液、カルボキシメチルセルロース、 10 ヒドロキシプロピルセルロース、メチルセルロース、ポリビニルピロリドンな どの結合剤、カルボキシメチルセルロースナトリウム、カルボキシメチルセル ロースカルシウム、低置換度ヒドロキシプロピルセルロース、乾燥デンプン、 アルギン酸ナトリウム、カンテン末、ラミナラン末、炭酸水素ナトリウム、炭 酸カルシウムなどの崩壊剤、ポリオキシエチレンソルビタン脂肪酸エステル類、 ラウリル硫酸ナトリウム、ステアリン酸モノグリセリドなどの界面活性剤、白 糖、ステアリン、カカオバター、水素添加油などの崩壊抑制剤、第4級アンモ ニウム塩基、ラウリル硫酸ナトリウムなどの吸収促進剤、グリセリン、デンプ ンなどの保湿剤、デンプン、乳糖、カオリン、ベントナイト、コロイド状ケイ 酸などの吸着剤、精製タルク、ステアリン酸塩、ホウ酸末、ポリエチレングリ コールなどの滑沢剤などを使用できる。更に錠剤は必要に応じ通常の剤皮を施 した錠剤、例えば糖衣錠、ゼラチン被包錠、腸溶被錠、フィルムコーティング 錠とすることができ、また二重錠ないしは多層錠とすることもできる。

丸剤の形態に成形するに際しては、製剤担体として例えばブドウ糖、乳糖、 25 デンプン、カカオ脂、硬化植物油、カオリン、タルクなどの賦形剤、アラビア ゴム末、トラガント末、ゼラチン、エタノールなどの結合剤、ラミナラン、カ ンテンなどの崩壊剤などを使用できる。

カプセル剤は、常法に従い通常本発明の有効成分を上記で例示した各種の製剤担体と混合して硬質ゼラチンカプセル、軟質カプセルなどに充填して調整さ

れる。

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経口投与用液体投与形態は、慣用される不活性希釈剤、例えば水、を含む医薬的に許容される溶液、エマルジョン、懸濁液、シロップ、エリキシルなどを包含し、更に湿潤剤、乳剤、懸濁剤などの助剤を含ませることができ、これらは常法に従い調製される。

非経口投与用の液体投与形態、例えば滅菌水性乃至非水性溶液、エマルジョン、懸濁液などへの調製に際しては、希釈剤として例えば水、エチルアルコール、プロピレングリコール、ポリエチレングリコール、エトキシ化イソステアリルアルコール、ポリオキシエチレンソルビタン脂肪酸エステル及びオリーブ油などの植物油などを使用でき、また注入可能な有機エステル類、例えばオレイン酸エチルなどを配合できる。これらには更に通常の溶解補助剤、緩衝剤、湿潤剤、乳化剤、懸濁剤、保存剤、分散剤などを添加することもできる。 滅菌は、例えばバクテリア保留フィルターを通過させる濾過操作、殺菌剤の配合、照射処理及び加熱処理などにより実施できる。また、これらは使用直前に滅菌水や適当な滅菌可能媒体に溶解することのできる滅菌固体組成物形態に調製することもできる。

坐剤や膣投与用製剤の形態に成形するに際しては、製剤担体として、例えばポリエチレングリコール、カカオ脂、高級アルコール、高級アルコールのエステル類、ゼラチン及び半合成グリセライドなどを使用できる。

20 ペースト、クリーム、ゲルなどの軟膏剤の形態に成形するに際しては、希釈剤として、例えば白色ワセリン、パラフイン、グリセリン、セルロース誘導体、プロピレングリコール、ポリエチレングリコール、シリコン、ベントナイト及びオリーブ油などの植物油などを使用できる。

経鼻又は舌下投与用組成物は、周知の標準賦形剤を用いて、常法に従い調製 25 することができる。

尚、本発明薬剤中には、必要に応じて着色剤、保存剤、香料、風味剤、甘味 剤などや他の医薬品などを含有させることもできる。

上記医薬製剤中に含有されるべき有効成分の量及びその投与量は、特に限定されず、所望の治療効果、投与法、治療期間、患者の年齢、性別その他の条件

などに応じて広範囲より適宜選択される。一般的には、投与量は、通常、1日当り体重60kg当り、約0.01mg~100mg、好ましくは約1mg~100mgとするのがよく、1日に1~数回に分けて投与することができる。

5 本明細書の配列表の配列番号は、以下の配列を示す。

〔配列番号:1〕

ヒト由来肝臓型グルコキナーゼをコードするDNAの塩基配列を示す。

[配列番号:2]

ヒト由来肝臓型グルコキナーゼのアミノ酸配列を示す。

10 〔配列番号:3〕

ヒト由来 β 細胞グルコキナーゼのアミノ酸配列を示す。

[配列番号:4]

ヒト由来肝臓型グルコキナーゼのN末端側のアミノ酸残基11個を欠失させたタンパク質をコードするDNAの塩基配列を示す。

15 〔配列番号:5〕

ヒト由来肝臓型グルコキナーゼのN末端側のアミノ酸残基11個を欠失させたタンパク質のアミノ酸配列を示す。

〔配列番号:6〕

以下の実施例1におけるPCR反応で使用した、プライマー1の塩基配列を 20 示す。

〔配列番号:7〕

以下の実施例1におけるPCR反応で使用した、プライマー2の塩基配列を示す。

〔配列番号:8〕

25 ヒト由来肝臓型グルコキナーゼのN末端側のアミノ酸残基15個を欠失させたタンパク質のアミノ酸配列を示す。

〔配列番号:9〕

以下の実施例6におけるPCR反応で使用した、プライマーの塩基配列を示す。

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[配列番号:10]

以下の実施例6におけるPCR反応で使用した、プライマーの塩基配列を示す。

5 (実施例)

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以下、本発明を、実施例を用いて具体的に説明する。

(変異型酵素の精製方法)

Human グルコキナーゼには、プロモーターの違いよって肝臓型と膵臓型が存在し、N末端の15残基が異なる。三次元構造解析を目的に結晶化を行うために、この部分の一部あるいはすべてを欠損した変異型酵素を以下の方法で作成した。

pCR2. 1 (INTROGEN 社製) 上にクローニングされた Human 肝臓型グルコキナーゼの cDNA と 2 種のプライマーセット

- 5' gtcacaaggagccagaagcttatggccttgactctggtag- 3'(配列番号6) 及び 15 5' -gaagccccacgacattgttcccttctgc - 3 (配列番号7)の組み合わせ、ならびに、
 - 5' ccaggcccagacagcctatggtagagcagatcc- 3'、 (配列番号9) 及び
 - 5' -gaagccccacgacattgttcccttctgc 3' (配列番号10)

を用いて PCR 反応を行った。得られた PCR 産物の Hind III、ClaI 断片を pFLAG・CTC ベクター (Eastman Kodak) の Hind III, Eco RI 部位にクローニングされていた肝臓型 GK の Hind III - Cla I 領域と置換することで、肝臓型 GK の $1\sim11$ 残基を欠損する変異型 GK(Δ 1-1 1)、及び $1\sim15$ 残基を欠損する変異型 GK(Δ 1-1 5)をコードする cDNA を得た。得られた cDNA の配列を確認した後、これらのベクターを発現ベクターとし、大腸菌 DH5 α 株(宝 酒造社製)を形質変換した。

形質変換体を LB 培地で 600nm の吸収が 0.8 になるまで 37 \mathbb{C} で培養した後、終濃度が 0.4mM になるようにイソプロピルー1-チオー $\beta-$ D-ガラクシド (和光純薬社製) を加え、25 \mathbb{C} で 16 時間、タンパク質の生産誘導を行った。

培養された大腸菌を遠心機で収集し、以下の成分を含む緩衝液(50 mM リン酸カリ (Potassium Phosphate) pH7.5, 50mM NaCl, 2 mM DTT, 0.5 mM Pefabloc SC (関東化学社製)、a proteinase inhibitor mixture (Roche 社製)) に懸濁した。

5 収集した大腸菌は、超音波破砕法によって破砕し、可溶化画分を上記の緩衝液に対して透析した後、HiTrapQカラム(アマシャム社製)により精製した。
HiTrapQカラムより塩化カリウムのグラジエントにより溶出された GK 画分を
希釈により塩濃度 50mM に希釈した。

希釈された GK 画分を論文 (Preparative Biochemistry, 20(2), 163-178 (1990)) に示されている方法で作製した Glucosamin Sepharose カラムにより精製した。 GK 画分を Glucosamin Sepharose カラムに吸着させ 100mM 塩化ナトリウムで不純物を除いた後、1M のグルコースにより溶出させた。

溶出された GK 画分は、MonoQ10/10 カラムにより精製した。MonoQ10/10 カラム (アマシャム社製) より塩化ナトリウムのグラジエントにより溶出された GK 画分を、移動層として 50mM Tris-Cl pH7. 2, <math>50mM NaCl 緩衝液を用いて、Superdex200 カラム (アマシャム社製) により精製した。

(結晶化方法)

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(変異型 GK (Δ1-11) /グルコース/化合物複合体の結晶)

20 変異型 $GK(\Delta 1-11)$ /グルコース/化合物複合体の結晶は、以下に示す蒸気拡散の手法を用いて得た。なお、変異型 $GK(\Delta 1-11)$ は、配列番号 5 で表されるアミノ酸配列を有するグルコキナーゼを意味する。

後に、試料溶液中に最大 $0.4 \text{ mm} \times 0.4 \text{ mm} \times 0.7 \text{ mm}$ 程度の結晶が得られた(実施例 1)。

さらに上記の方法で得られた結晶を下記化合物 2 (式III b で表される化合物) が0.3 mMの濃度で含まれるようにして、28~30% PEG 1500、0.1 M Hepes - NaOH (pH6.6)溶液に3~7日程度浸透することによって、下記化合物 2 と上記変異型GKの複合体結晶を得た(実施例 2)。

化合物1

10 化合物 2

また、前記化合物1に代えて化合物3(式 III c で表される化合物)を用いた以外は、実施例1と同様にして結晶化を試みた結果、それぞれ実施例1と同様な結晶が得られた(実施例3)。

化合物3

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得られた結晶を10%のグリセロールを加えた結晶化溶液に浸し、続いて液体窒素中で急速に凍結した。シンクロトロン施設 KEK-PF の BL6B において振動法により、凍結した結晶の X 線回折データを 100K 窒素気流中で収集した。得られた回折像から、DENZO/SCALEPACK(HKL 社製)を用いて回折強度を数値化し、結晶構造因子を求めた。この段階で結晶は六方晶系で空間群は $P6_522$ あるいは $P6_122$ を有し、結晶の単位格子は、a=b=79.9 オングストローム,c=322.2 オングストローム, $\alpha=\beta=90^\circ$, $\gamma=120^\circ$ であるとわかった。

得られた構造因子と Human ヘキソキナーゼ タイプ1の3次元構造座標を用いて分子置換法を行い構造を解析した。計算には8オングストロームから4オングストロームの分解能のデータを用い、CCP4 (Council for the Central laboratory of the Research Councils) の Amore プログラムにより行った。計算により得られた構造のR因子は、53.7%であり、結晶の空間群はP 6_5 22で非対称単位に変異型 GK 一分子を含むことが分かった。この構造と構造因子から電子密度マップを得て、プログラム 0 (Dat-ONO 社製) を用いて変異型グルコキナーゼの構造を決定した。

次に CNX(Accelrys Inc.)を用いてアミノ酸の位置の精密化を行い、プログラム 0 を用いてアミノ酸残基の同定を行った。この操作を繰り返し行い、変異型グルコキナーゼのスレオニン 14 からシステイン 461 までの 448 アミノ酸残基の構造座標、1 分子のグルコース分子、1 分子の化合物 A、1 個のナトリウムイオン、及び 149 個の水分子を同定し構造座標を決定した。最終的に決定された構造の正確さの指標とされる R 因子は、30 オングストロームから 2.3 オングストロームの分解能のデータに対して R=23.2%であり、構造の精密化の段階で計算に用いなかったデータに対する R 因子 (Rfree) は 27.4%であった。

ラマチャンドラン・プロットで確認したところ許容されない構造を持ったアミノ酸残基はなかった。

決定された変異型グルコキナーゼの構造は、アイソザイムであるヘキソキナーゼの構造と似たものであったが、グルコキナーゼを活性化する化合物1(式 IIIaの化合物)の結合している部位の構造は異なっていた。この構造の相違は、現在の計算化学の能力で予想できうるものでなく、今回の構造解析により、この部位がアクティベーターの結合部位であること、そしてその詳細な立体構造が初めて明らかとなった。図1 a は、ここで解明されたグルコキナーゼの三次元構造を示すリボン図である。図1 a に示されるように、新規に見つかった アクティベーター結合部位は、ラージドメインとスモールドメインの間に位置しており、基質であるグルコースが結合しているグルコキナーゼの活性中心から、約20 オングストローム離れていた。アクティベーター結合部位を構成しているグルコキナーゼのアミノ酸残基は以下のとおりであった。チロシン61~セリン69、グルタミン酸96~グルタミン98、イソロイシン159、メチオニン210~チロシン215、ヒスチジン218~グルタミン酸221、メチオニン235、アルギニン250、ロイシン451~リジン459。

また、この結合部位に対する化合物1(式 IIIa の化合物)の結合様式を図2に、グルコキナーゼの結合部位の構造を図3に示す。チアゾール環は、バリン62、バリン452、バリン455のそれぞれのアミノ酸側鎖の分子とファンデルワールス接触をしており、またチアゾール環上の窒素原子がアルギニン63の主鎖の窒素原子と水素結合をしていた。化合物1上のアミドの窒素原子は、アルギニン63の主鎖の酸素原子と水素結合をしていた。化合物1のベンゼン環部分はイソロイシン211とファンデルワールス接触をしており、ベンゼン環に置換したフッ素原子はチロシン214の側鎖とファンデルワールス接触をしていた。化合物1のアニリン構造は、チロシン215の側鎖の酸素原子と水素結合を形成していた。硫黄を介してベンゼン環と結合しているイミダゾール環部分は、メチオニン210、メチオニン235、チロシン214のアミノ酸側鎖部分とファンデルワールス接触をしていた。ラージドメインとスモールドメインを結んでいる、セリン64~セリン69の部分は、溶液に露出した構造をしており、化合物

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1は、この部分が形作るアーチ状構造の下部に結合していた(図3)。

(実施例4:ドラッグデザインの実施例)

ソフトウエア UNITY (トライポス社製)を用い、Arg63の主鎖 NH, COからそれぞれ発生させた水素結合アクセプター、水素結合ドナーのファルマコフォアと、複合体を形成するリガンドのアニリン部分のフェニル基に相当する空間に形成された疎水性のファルマコフォア、および蛋白の構造を元に作成した蛋白表面を検索条件としてライブラリ化合物をスクリーニングし、下記化合物 4、及び化合物 5 が得られ、アッセイを行ったところ、それぞれ 7 8 0 %、および 5 6 0 %の活性が認められた。なお活性が 7 8 0 %とは、グルコキナーゼの活性をコントロールを 1 0 0 %としたときに、これらの化合物によって 7 8 0 %まで増強されたことを示す (グルコース 2.5M 及びリガンド 10 μ M を使用)。

化合物 4

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化合物5

$$\begin{array}{c|c} S & & & \\ \hline \\ N & & \\ NH_2 & & \\ \end{array}$$

活性:560%

20 (実施例5)

(変異型 GK (Δ1-15) の結晶)

変異型 $GK(\Delta 1-15)$ (配列番号 8 で表されるアミノ酸配列を有するグルコキナーゼ) の単体の結晶は、以下に示す蒸気拡散の手法を用いて得た。

すなわち、高純度に精製された変異型 GK を濃縮し、最終的に 10mg/ml 程度の変異型 GK の溶液 (25 mM Tris-Cl pH7. 2, 50 mM NaCl, 5 mM TCEP) とした。 タンパク質溶液 1~5 μ l に結晶化溶液 (1.5 ~ 1.6 M 硫酸アンモニウム、50mM NaCl、0.1 M Bicine NaOH (pH8.7)) を等量加えて混合した溶液を 0.5~1ml の結晶化溶液が入った密閉容器に、両溶液が触れ合わないように収め、20℃で静置した。およそ 3 日~1 ヶ月の静置の後に、試料溶液中に最大 0.07mm×0.5mm 程度の大きさの結晶が得られた。

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次に、CNX(モレキュラーシミュレーション社製)を用いてアミノ酸の位置 の精密化を行い、プログラム0を用いてアミノ酸残基の同定を行った。この操作を繰り返し行い、変異型グルコキナーゼのメチオニン15からヒスチジン156とアスパラギン180からシステイン461までの424アミノ酸残基の構造座標、2分子の硫酸イオン、1個のナトリウムイオン、及び7個の水分子を同定し構造座標を決定した。最終的に決定された構造の正確さの指標とされる8因

子は、50~3.4 オングストロームの分解能のデータに対して R=23.8%であり、 構造の精密化の段階で計算に用いなかったデータに対する R 因子 (Rfree) は 30.6%であった。ラマチャンドラン・プロットで確認したところ、許容されな い構造を持ったアミノ酸残基はなかった。

図1a及び図1bに、それぞれグルコキナーゼ(Δ1-11)/グルコース/化 5 合物1の構造を示すリボン図、及びグルコキナーゼ(△1-15)単体の構造を 示すリボン図を示す。なお、右図は、左図を回転した図である。決定された変 異型 $GK(\Delta 1-15)$ 単体の構造においてラージドメイン及びスモールドメ インの主要部分の構造は、変異型 $GK(\Delta 1-11)$ / グルコース/化合物複 合体結晶により決定されたグルコキナーゼにおけるそれぞれの構造と似たもの 10 であったが、2つのドメインの相対位置が大きく異なっていた。変異型 GK (△ 1-15) 単体構造においてスモールドメインの主要部分は、変異型 GK(△ 1-11) /グルコース/化合物複合体構造におけるスモールドメインの位置 からおよそ 99 度回転していた。また、グルコキナーゼの C 末端領域に位置し 変異型 GK (Δ1-11) /グルコース/化合物複合体構造においてはスモー 15 ルドメインを構成していた α 1 3 ヘリックスは、変異型 GK (Δ 1 - 1 5) 単 体構造においてはもはやスモールドメインを構成せず、両ドメイン間に位置し ていた。さらに、変異型 $GK(\Delta 1 - 11)$ /グルコース/化合物複合体構造 における基質グルコースの結合部位及び活性化剤結合部位はどちらも2つのド メイン間に存在していたため、新たに決定した構造ではそれらの部位の構造は 20 大きく変化していた。変異型 GK (Δ1-15) 単体構造では酵素活性に重要 な役割を果たすアミノ酸残基が活性部位を形成しておらず、今回解析した変異 型 GK (Δ1-15) 単体の構造は、グルコキナーゼの不活性状態の構造であ った。また、変異型 GK (Δ1-15) 単体の構造において活性化剤結合部位 は、完全に消失していた。変異型 $GK(\Delta 1 - 11)$ /グルコース/化合物複 25 合体構造および変異型 $GK(\Delta 1-15)$ 単体構造により観測されたグルコキ ナーゼの構造変化(約99度のドメインの回転)は、今まで知られていたヘキソ キナーゼの構造変化(約12度のドメインの回転)と比較してはるかに大きな

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ものであり、現在の計算化学の能力で予想でき得るものではなく、今回の構造 解析により初めて明らかとなったものである。

また、不活性型である変異型 $GK(\Delta 1-15)$ 単体構造への構造変化を阻害する目的として、変異型 $GK(\Delta 1-11)$ / グルコース/ 化合物複合体構造で示された化合物結合部位に結合する化合物を設計することにより、グルコキナーゼの活性化剤を設計できることが明らかとなった。

産業上の利用可能性

以上説明したように、本発明によれば、従来は結晶化が困難であったグルコキナーゼタンパク質の結晶を得ることができた。この結晶の構造を解析することによって得られる三次元構造座標は、グルコキナーゼに結合する化合物を設計するために好適に用いることができる。また、このようにして設計される化合物は、グルコキナーゼに結合するので、グルコキナーゼ活性化剤又は阻害剤として、グルコキナーゼ活性が関与する疾患の治療剤(例えば、糖尿病治療15 剤)として用いることができる。

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請求の範囲

- 1. 結晶化に用いることを特徴とする、グルコキナーゼタンパク質。
- 2. 配列番号5に記載のアミノ酸配列からなることを特徴とする、請求項1
- 5 に記載のタンパク質。
 - 3. 配列番号5に記載のアミノ酸配列又はそのアミノ酸配列と実質的に同一のアミノ酸配列からなることを特徴とするタンパク質の結晶。
 - 4. 前記タンパク質がグルコキナーゼタンパク質である、請求項3に記載の結晶。
- 10 5. 配列番号5に記載のアミノ酸配列を有するタンパク質の結晶である、請求項3に記載の結晶。
 - 6. 格子定数が、下記式(1)~(4): a=b=79.9±4オングストローム …(1) c=322.2±15オングストローム …(2)
- 15 $\alpha = \beta = 90^{\circ}$... (3) $\gamma = 120^{\circ}$... (4)

を満たす、請求項3に記載の結晶。

- 7. 空間群がP6522である、請求項6に記載の結晶。
- 8. 表1に記載の三次元構造座標データによって特定されるタンパク質の結
- 20 晶。
- 25 グストローム以下である結晶。
 - 10. 化合物結合部位が、配列番号5に示すアミノ酸配列における、チロシン61~セリン69、グルタミン酸96~グルタミン98、イソロイシン159、メチオニン210~チロシン215、ヒスチジン218~グルタミン酸221、メチオニン235、アルギニン250、ロイシン451~リジン459

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のアミノ酸残基の少なくともひとつによって構成されている、請求項3~9の いずれかに記載の結晶。

- 11. 配列番号5に記載のアミノ酸配列又はそのアミノ酸配列と実質的に同一のアミノ酸配列からなるタンパク質と該タンパク質に結合可能な化合物との を含む結晶。
 - 12. 前記化合物が、式(I)で表される、請求項11に記載の結晶。

(l)

[式中、 R^1 は、 Λ ロゲン原子、-S-(O)p-A、-S-(O)q-B又は-O10 -Bを示し(ここで、p及びqは同一又は異なって、 $0\sim 2$ の整数を示し、Aは置換されていてもよい直鎖の C_1-C_8 アルキル基を示し、Bは置換されていてもよい五負環又は六員環のアリール基又はヘテロアリール基を示し、 R^2 は水素原子又は Λ ロゲン原子を示し、



15 (11)

は、アミド基に結合した炭素原子の隣に窒素原子を有する、置換されていても よい単環の又は双環のヘテロアリール基を示す)

13. 前記化合物が、式(IIIa)~式(IIIc)で表されるいずれかの化合物である請求項12に記載の結晶。

5

$$0 = \stackrel{\mathsf{CH}_3}{=} 0 \qquad 0 \qquad \stackrel{\mathsf{S}}{=} \mathsf{CH}_3$$
 (IIIc)

14. 配列番号8に記載のアミノ酸配列からなることを特徴とする、請求項1に記載のタンパク質。

- 15. 配列番号8に記載のアミノ酸配列又はそのアミノ酸配列と実質的に同 0 一のアミノ酸配列からなることを特徴とするタンパク質の結晶。
 - 16. 前記タンパク質がグルコキナーゼタンパク質である、請求項15に記載の結晶。
 - 17. 配列番号8に記載のアミノ酸配列を有するタンパク質の結晶である、請求項15に記載の結晶。
- 15 18. 格子定数が、下記式 a=b=103.2±5オングストローム … (5) c=281.0±7オングストローム … (6)

$$\alpha = \beta = 90^{\circ} \quad \cdots \quad (7)$$

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 $\gamma = 120^{\circ} \quad \cdots \quad (8)$

を満たす、請求項15に記載の結晶。

- 19. 空間群が P6,22 である、請求項18 に記載の結晶。
- 20. 表2に記載の三次元構造座標データによって特定されるタンパク質の 結晶。
- 21. 表2に記載の三次元構造座標データの少なくとも一つのデータを変更した三次元構造座標データにおいて、表2に記載の三次元構造座標データで示されるアミノ酸の主鎖の原子(Cα原子)と、該Cα原子と対応する前記変更した三次元構造座標データで示されるCα原子との平均二乗偏差が、0.6オングストローム以下である結晶。
 - 22. 配列番号 2 に記載のアミノ酸配列を有するタンパク質のN末端、C末端のいずれかまたは両方から、 $1\sim5$ 0 個のアミノ酸残基を欠損したアミノ酸配列を有するタンパク質を製造するタンパク質製造工程と、

前記タンパク質製造工程で得られたタンパク質と結合する化合物と、前記タ 15 ンパク質製造工程で得られたタンパク質とを反応させるタンパク質反応工程と を含む、

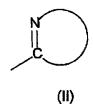
タンパク質及びそのタンパク質と結合する化合物の複合体を含む結晶の製造 方法。

- 23. タンパク質の結晶を製造する方法であって、
- 20 配列番号 5 に記載のアミノ酸配列又はそのアミノ酸配列と実質的に同一のアミノ酸配列を含みグルコキナーゼ活性を有するタンパク質、及び該タンパク質に結合可能な化合物を用いることを特徴とする、結晶の製造方法。
 - 24. 前記タンパク質に結合可能な化合物が、式(I)で表される化合物であることを特徴とする、請求項23に記載のタンパク質の結晶の製造方法。

$$R^1$$
 N
 C
 NH_2

(1)

[式中、 R^1 は、Nロゲン原子、-S-(O)p-A、-S-(O)q-B又は-O-Bを示し(ここで、p及びqは同一又は異なって、 $0\sim2$ の整数を示し、Aは置換されていてもよい直鎖の C_1-C_6 アルキル基を示し、Bは置換されていてもよい五員環又は六員環のアリール基又はヘテロアリール基を示し、 R^2 は水素原子又はNロゲン原子を示し、



は、アミド基に結合した炭素原子の隣に窒素原子を有する、置換されていても 10 よい単環の又は双環のヘテロアリール基を示す)

25. 共結晶法又はソーキング法による、請求項23、又は請求項24に記載の結晶の製造方法。

26. タンパク質の立体構造情報に基づいて該タンパク質に結合する化合物 の構造をデザインするドラッグデザイン方法であって、

15 該タンパク質の立体構造情報が、請求項3~13、請求項15~21のうちの いずれか一項に記載の結晶を解析することによって得られる情報であることを 特徴とする、ドラッグデザイン方法。

27. 前記立体構造情報に基づいて、前記タンパク質の化合物結合部位を推測する結合部位推測工程と、

20 前記結合部位推測工程で推測された化合物結合部位に適合する化合物を、化合

物ライブラリより選択する選択工程と、

を含むことを特徴とする、請求項26に記載のドラッグデザイン方法。

- 28. 前記立体構造情報に基づいて、前記タンパク質の化合物結合部位を推測する結合部位推測工程と、
- 5 前記結合部位推測工程で推測された化合物結合部位に適合する化合物の構造を構築する化合物構造構築工程と、

を含むことを特徴とする、請求項26に記載のドラッグデザイン方法。

- 29. 前記立体構造情報に基づいて、前記タンパク質の化合物結合部位を推測する結合部位推測工程と、
- 10 前記結合部位推測工程で推測された化合物結合部位と該化合物結合部位に適合 する化合物とが相互作用するように化合物の構造を目視によりデザインするデ ザイン工程と、

を含むことを特徴とする、請求項26に記載のドラッグデザイン方法。

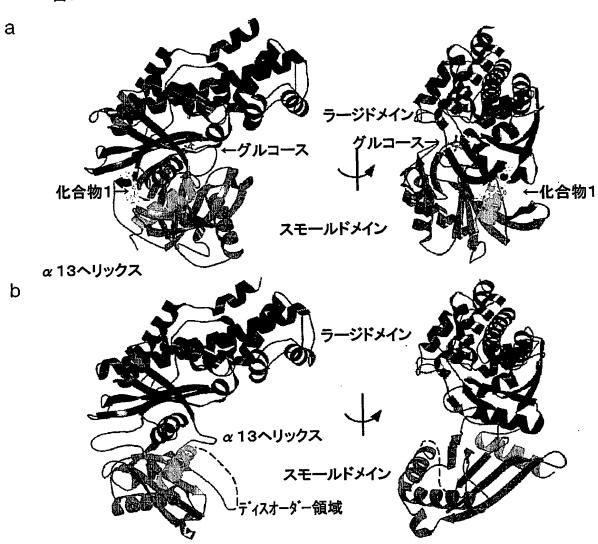
- 30. 前記化合物結合部位が、配列番号5に示すアミノ酸配列における、チロシン61~セリン69、グルタミン酸96~グルタミン98、イソロイシン159、メチオニン210~チロシン215、ヒスチジン218~グルタミン酸221、メチオニン235、アルギニン250、ロイシン451~リジン459のアミノ酸残基の少なくともひとつによって構成されている、請求項26~29のうちのいずれか一項に記載のドラッグデザイン方法。
- 20 31. さらに、前記化合物結合部位に適合すると推定される候補化合物の生理活性を測定する工程を含む、請求項26~30のいずれか一項に記載のドラッグデザイン方法。
- 32. さらに、前記化合物結合部位に適合すると推定される候補化合物と、 配列番号5に記載のアミノ酸配列又はそのアミノ酸配列と実質的に同一のアミ ノ酸配列を含むタンパク質とを接触させ、その候補化合物が該タンパク質に結 合するか否か判定する結合判定工程を含む、請求項26~30のいずれか一項 に記載のドラッグデザイン方法。
 - 33. 請求項26~30のいずれか一項に記載のドラッグデザイン方法によって選択された化合物群を化合物アレイとして組み合わせることを含む化合物

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アレイの製造方法。

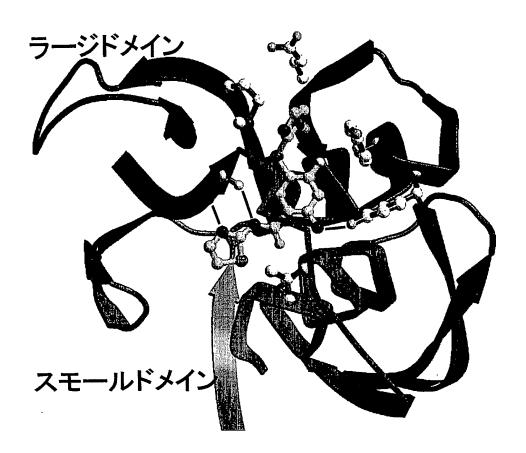
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図1



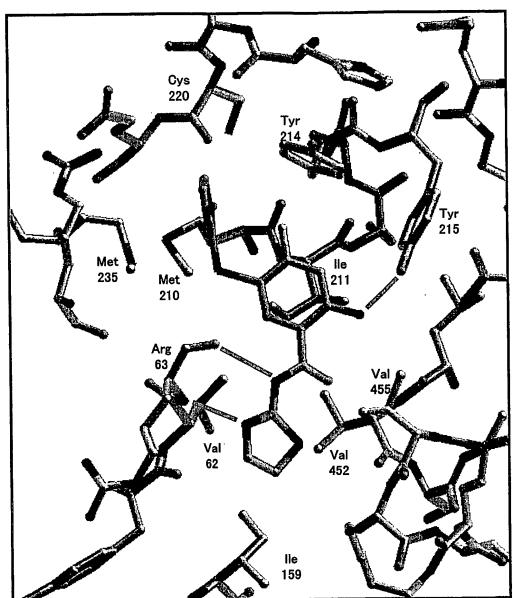
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図2



3/3

図3



1/15 SEQUENCE LISTING

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2/15

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Lys Val Met Arg Arg Met Gln Lys Glu Met Asp Arg Gly Leu Arg Leu 35 40 45

Glu Thr His Glu Glu Ala Ser Val Lys Met Leu Pro Thr Tyr Val Arg 50 55 60

Ser Thr Pro Glu Gly Ser Glu Val Gly Asp Phe Leu Ser Leu Asp Leu 65 70 75 80

								3/1	5							
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Glu	Asp	Ala 115	Met	Thr	Gly	Thr	Ala 120	Glu	Met	Leu	Phe	Asp 125	Tyr	Ile	Ser	
Glu	Cys 130	Ile	Ser	Asp	Phe	Leu 135	Asp	Lys	His	Gln	Met 140	Lys	His	Lys	Lys	
Leu 145	Pro	Leu	Gly	Phe	Thr 150	Phe	Ser	Phe	Pro	Val 155	Arg	His	Glu	Asp	Ile 160	
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Glu	Trp	Gly	Ala 260	Phe	Gly	Asp	Ser	Gly 265	Glu	Leu	Asp	Glu	Phe 270	Leu	Leu	

4/15

Glu Tyr Asp Arg Leu Val Asp Glu Ser Ser Ala Asn Pro Gly Gln Gln 275 280 285

- Leu Tyr Glu Lys Leu Ile Gly Gly Lys Tyr Met Gly Glu Leu Val Arg 290 295 300
- Leu Val Leu Leu Arg Leu Val Asp Glu Asn Leu Leu Phe His Gly Glu 305 310 315 320
- Ala Ser Glu Gln Leu Arg Thr Arg Gly Ala Phe Glu Thr Arg Phe Val 325 330 335
- Ser Gln Val Glu Ser Asp Thr Gly Asp Arg Lys Gln Ile Tyr Asn Ile 340 345 350
- Leu Ser Thr Leu Gly Leu Arg Pro Ser Thr Thr Asp Cys Asp Ile Val 355 360 365
- Arg Arg Ala Cys Glu Ser Val Ser Thr Arg Ala Ala His Met Cys Ser 370 375 380
- Ala Gly Leu Ala Gly Val Ile Asn Arg Met Arg Glu Ser Arg Ser Glu 385 390 395 400
- Asp Val Met Arg Ile Thr Val Gly Val Asp Gly Ser Val Tyr Lys Leu 405 410 415
- His Pro Ser Phe Lys Glu Arg Phe His Ala Ser Val Arg Arg Leu Thr 420 425 430
- Pro Ser Cys Glu Ile Thr Phe Ile Glu Ser Glu Glu Gly Ser Gly Arg 435 440 445
- Gly Ala Ala Leu Val Ser Ala Val Ala Cys Lys Lys Ala Cys Met Leu 450 455 460

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Gly Gln

465

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<211> 465

<212> PRT

<213> Homo sapiens

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Val Met Arg Arg Met Gln Lys Glu Met Asp Arg Gly Leu Arg Leu Glu 35 40 45

Thr His Glu Glu Ala Ser Val Lys Met Leu Pro Thr Tyr Val Arg Ser 50 55 60

Thr Pro Glu Gly Ser Glu Val Gly Asp Phe Leu Ser Leu Asp Leu Gly 65 70 75 80

Gly Thr Asn Phe Arg Val Met Leu Val Lys Val Gly Glu Glu Glu 85 90 95

Gly Gln Trp Ser Val Lys Thr Lys His Gln Met Tyr Ser Ile Pro Glu 100 105 110

Asp Ala Met Thr Gly Thr Ala Glu Met Leu Phe Asp Tyr Ile Ser Glu 115 120 125

Cys Ile Ser Asp Phe Leu Asp Lys His Gln Met Lys His Lys Lys Leu 130 135 140

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Pro 145	Leu	Gly	Phe	Thr	Phe 150	Ser	Phe	Pro	Val	Arg 155	His	Glu	Asp	Ile	Asp 160
Lys	Gly	Ile	Leu	Leu 165	Asn	Trp	Thr	Lys	Gly 170	Phe	Lys	Ala	Ser	Gly 175	Ala
Glu	Gly	Asn	Asn 180	Val	Val	Gly	Leu	Leu 185	Arg	Asp	Ala	Ile	Lys 190	Arg	Arg
Gly	Asp	Phe 195	Glu	Met	Asp	Val	Val 200	Ala	Met	Val	Asn	Asp 205	Thr	Val	Ala
Thr	Met 210	Ile	Ser	Cys	Tyr	Tyr 215	Glu	Asp	His	Gln	Cys 220	G1u	Val	Gly	Met
Ile 225	Val	Gly	Thr	Gly	Cys 230	Asn	Ala	Cys	Tyr	Met 235	Glu	G1u	Met	Gln	Asn 240
Val	Glu	Leu	Val	G1u 245	Gly	Asp	Glu	Gly	Arg 250	Met	Cys	Val	Asn	Thr 255	Glu
Trp	Gly	Ala	Phe 260	Gly	Asp	Ser	Gly	Glu 265	Leu	Asp	Glu	Phe	Leu 270	Leu	Glu
Tyr	Asp	Arg 275	Leu	Val	Asp	Glu	Ser 280	Ser	Ala	Asn	Pro	Gly 285	Gln	Gln	Leu
Tyr	Glu 290	Lys	Leu	Ile	Gly	Gly 295	Lys	Tyr	Met	Gly	G1u 300	Leu	Val	Arg	Leu
Val 305	Leu	Leu	Arg	Leu	Val 310	Asp	Glu	Asn	Leu	Leu 315	Phe	His	Gly	Glu	Ala 320
Ser	Glu	Gln	Leu	Arg 325	Thr	Arg	Gly	Ala	Phe 330	Glu	Thr	Arg	Phe	Va l 335	Ser

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Gln Val Glu Ser Asp Thr Gly Asp Arg Lys Gln Ile Tyr Asn Ile Leu 340 345 350

Ser Thr Leu Gly Leu Arg Pro Ser Thr Thr Asp Cys Asp Ile Val Arg 355 360 365

Arg Ala Cys Glu Ser Val Ser Thr Arg Ala Ala His Met Cys Ser Ala 370 375 380

Gly Leu Ala Gly Val Ile Asn Arg Met Arg Glu Ser Arg Ser Glu Asp 385 390 395 400

Val Met Arg Ile Thr Val Gly Val Asp Gly Ser Val Tyr Lys Leu His 405 410 415

Pro Ser Phe Lys Glu Arg Phe His Ala Ser Val Arg Arg Leu Thr Pro 420 425 430

Ser Cys Glu Ile Thr Phe Ile Glu Ser Glu Glu Gly Ser Gly Arg Gly 435 440 445

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Gln

465

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<212> DNA

<213> Homo sapiens

⟨400⟩ 4

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8/15

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<210> 5 <211> 455 <212> PRT

<213> Homo sapiens

<400> 5

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1 5 10 15

Glu Glu Asp Leu Lys Lys Val Met Arg Arg Met Gln Lys Glu Met Asp 20 25 30

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Arg Gly Leu Arg Leu Glu Thr His Glu Glu Ala Ser Val Lys Met Leu 35 40 45

- Pro Thr Tyr Val Arg Ser Thr Pro Glu Gly Ser Glu Val Gly Asp Phe 50 55 60
- Leu Ser Leu Asp Leu Gly Gly Thr Asn Phe Arg Val Met Leu Val Lys 65 70 75 80
- Val Gly Glu Gly Glu Gly Gln Trp Ser Val Lys Thr Lys His Gln 85 90 95
- Met Tyr Ser Ile Pro Glu Asp Ala Met Thr Gly Thr Ala Glu Met Leu 100 105 110
- Phe Asp Tyr Ile Ser Glu Cys Ile Ser Asp Phe Leu Asp Lys His Gln 115 120 125
- Met Lys His Lys Lys Leu Pro Leu Gly Phe Thr Phe Ser Phe Pro Val 130 · 135 140
- Arg His Glu Asp Ile Asp Lys Gly Ile Leu Leu Asn Trp Thr Lys Gly 145 150 155 160
- Phe Lys Ala Ser Gly Ala Glu Gly Asn Asn Val Val Gly Leu Leu Arg 165 170 175
- Asp Ala Ile Lys Arg Arg Gly Asp Phe Glu Met Asp Val Ala Met 180 185 190
- Val Asn Asp Thr Val Ala Thr Met Ile Ser Cys Tyr Tyr Glu Asp His 195 200 205
- Gln Cys Glu Val Gly Met Ile Val Gly Thr Gly Cys Asn Ala Cys Tyr 210 215 220

															•
								10/	15						
Met 225	Glu	Glu	Met	Gln	Asn 230	Val	Glu	Leu	Val	Glu 235	Gly	Asp	Glu	Gly	Arg 240
Met	Cys	Val	Asn	Thr 245	G1u	Trp	Gly	Ala	Phe 250	Gly	Asp	Ser	Gly	G1u 255	Leu
Asp	Glu	Phe	Leu 260	Leu	Glu	Tyr	Asp	Arg 265	Leu	Val	Asp	Glu	Ser 270	Ser	Ala
Asn	Pro	Gly 275	Gln	Gln	Leu	Tyr	Glu 280	Lys	Leu	Ile	Gly	Gly 285	Lys	Tyr	Met
Gly	G1u 290	Leu	Val	Arg	Leu	Val 295	Leu	Leu	Arg	Leu	Val 300	Asp	Glu	Asn	Leu
Leu 305	Phe	His	Gly	Glu	Ala 310	Ser	Glu	Gln	Leu	Arg 315	Thr	Arg	Gly	Ala	Phe 320
Glu	Thr	Arg	Phe	Val 325	Ser	Gln	Val	Glu	Ser 330		Thr	Gly	Asp	Arg 335	Lys
Gln	Ile	Tyr	Asn 340		Leu	Ser	Thr	Leu 345		Leu	Arg	Pro	Ser 350		Thr
Asp	Cys	Asp 355	Ile		Arg						Val	Ser 365		Arg	Ala
Ala	His 370		Cys	Ser	Ala	Gly 375		Ala	Gly	Val	Ile 380		Arg	Met	Arg
Glu 385		Arg	s Ser	Glu	Asp 390		Met	Arg	: Ile	Thr 395		Gly	Val	Asp	Gly 400

Ser Val Tyr Lys Leu His Pro Ser Phe Lys Glu Arg Phe His Ala Ser

405

410

415

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Val Arg Arg Leu Thr Pro Ser Cys Glu Ile Thr Phe Ile Glu Ser Glu 420 425 430

Glu Gly Ser Gly Arg Gly Ala Ala Leu Val Ser Ala Val Ala Cys Lys 435 440 445

Lys Ala Cys Met Leu Gly Gln 450 455

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28

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12/15

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35 40 45

Arg Ser Thr Pro Glu Gly Ser Glu Val Gly Asp Phe Leu Ser Leu Asp 50 55 60

Leu Gly Gly Thr Asn Phe Arg Val Met Leu Val Lys Val Gly Glu Gly 65 70 75 80

Glu Glu Gly Gln Trp Ser Val Lys Thr Lys His Gln Met Tyr Ser Ile 85 90 95

Pro Glu Asp Ala Met Thr Gly Thr Ala Glu Met Leu Phe Asp Tyr Ile 100 105 110

Ser Glu Cys Ile Ser Asp Phe Leu Asp Lys His Gln Met Lys His Lys 115 120 125

Lys Leu Pro Leu Gly Phe Thr Phe Ser Phe Pro Val Arg His Glu Asp 130 135 140

Ile Asp Lys Gly Ile Leu Leu Asn Trp Thr Lys Gly Phe Lys Ala Ser 145 150 155 160

Gly Ala Glu Gly Asn Asn Val Val Gly Leu Leu Arg Asp Ala Ile Lys 165 170 175

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Arg	Arg	Gly	Asp 180	Phe	Glu	Met	Asp	Val 185	Val	Ala	Met	Val	Asn 190	Asp	Thr
Val	Ala	Thr 195	Met	Ile	Ser	Cys	Tyr 200	Tyr	Glu	Asp	His	Gln 205	Cys	Glu	Val
Gly	Met 210	Ile	Val	Gly	Thr	Gly 215	Cys	Asn	Ala	Cys	Tyr 220	Met	Glu	Glu	Met
G1n 225	Asn	Val	Glu	Leu	Val 230	Glu	Gly	Asp	Glu	Gly 235	Arg	Met	Cys	Val	Asn 240
Thr	Glu	Trp	Gly	Ala 245	Phe	Gly	Asp	Ser	Gly 250	Glu	Leu	Asp	Glu	Phe 255	Leu
Leu	Glu	Tyr	Asp 260	Arg	Leu	Val	Asp	Glu 265	Ser	Ser	Ala	Asn	Pro 270	Gly	Gln
Gln	Leu	Tyr 275	Glu	Lys	Leu	Ile	Gly 280	Gly	Lys	Tyr	Met	Gly 285	Glu	Leu	Val
Arg	Leu 290	Val	Leu	Leu	Arg	Leu 295	Val	Asp	Glu	Asn	Leu 300	Leu	Phe	His	Gly
G1u 305	Ala	Ser	Glu	Gln	Leu 310	Arg	Thr	Arg	Gly	Ala 315	Phe	G1u	Thr	Arg	Phe 320
Val	Ser	Gln	Val	Glu 325	Ser	Asp	Thr	Gly	Asp 330	Arg	Lys	Gln	He	Tyr 335	Asn
Ile	Leu	Ser	Thr 340	Leu	Gly	Leu	Arg	Pro 345	Ser	Thr	Thr	Asp	Cys 350	Asp	Ile
Val	Arg	Arg 355	Ala	Cys	Glu	Ser	Val 360	Ser	Thr	Arg	Ala	A1a 365	His	Met	Cys

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Ser Ala Gly Leu Ala Gly Val Ile Asn Arg Met Arg Glu Ser Arg Ser 370 375 380

Glu Asp Val Met Arg Ile Thr Val Gly Val Asp Gly Ser Val Tyr Lys 385 390 395 400

Leu His Pro Ser Phe Lys Glu Arg Phe His Ala Ser Val Arg Arg Leu 405 410 415

Thr Pro Ser Cys Glu Ile Thr Phe Ile Glu Ser Glu Glu Gly Ser Gly
420 425 430

Arg Gly Ala Ala Leu Val Ser Ala Val Ala Cys Lys Lys Ala Cys Met 435 440 445

Leu Gly Gln 450

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<211> 38

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:Primer

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38

⟨210⟩ 10

⟨211⟩ 28

<212> DNA

<213> Artificial Sequence

15/15

<220>

<223> Description of Artificial Sequence:Primer

<400> 10

gaagccccac gacattgttc ccttctgc

28

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP03/06054

A. CLASS	DIFICATION OF SUBJECT MATTER C1 ⁷ C12N9/12, C12Q1/48					
Int.	C1' C12N9/12, C12Q1/48					
According t	o International Patent Classification (IPC) or to both na	ational classification and IPC				
B. FIELD	S SEARCHED					
Minimum d	ocumentation searched (classification system followed	by classification symbols)				
Int.	C17 C12N9/12, C12Q1/48		V			
Documentat	ion searched other than minimum documentation to the	e extent that such documents are included	in the fields searched			
	ata base consulted during the international search (nam		rch terms used)			
	TN), BIOSIS (DIALOG), WPI (DIALO SProt/PIR/Genbank/EMBL/DDBJ/Ge					
525	21200, 1111, 0011241112, 211212, 2020, 00	.neseq				
C DOCK	MENTE CONGINERED TO BE BELLEVANT					
C. DOCO	MENTS CONSIDERED TO BE RELEVANT					
Category*	Citation of document, with indication, where ap	ppropriate, of the relevant passages	Relevant to claim No.			
$\frac{X}{A}$	TANIZAWA, Y. et al., Human L.		<u>1</u>			
A	Gene: Cloning and Sequence De		2-25			
	Alternatively Spliced cDNAs, USA., 1991, Vol.88, pages 729					
	obii., 1991, voi.uu, pages 72.	74 60 7237				
A	MAHALINGAM B. et al., Structu		1-25			
	glucokinase in complex with					
	Diabetes, 1999, Vol.48, pages 1698 to 1705					
A	WILLSON M. et al., Yeast hexo	okinase inhibitors	1-25			
	designed from the 3-D enzyme	structure reboilding.				
	J. Enzyme Inhib., 1997, Vol.:	12, No.2, pages 101				
	to 121					
,						
Ì		ļ				
		·				
Furthe	er documents are listed in the continuation of Box C.	See patent family annex.				
	categories of cited documents:	"T" later document published after the inte				
	ent defining the general state of the art which is not red to be of particular relevance	priority date and not in conflict with th understand the principle or theory under				
	document but published on or after the international filing	"X" document of particular relevance; the c	claimed invention cannot be			
"L" docume	ent which may throw doubts on priority claim(s) or which is	considered novel or cannot be consider step when the document is taken alone				
	establish the publication date of another citation or other reason (as specified)	"Y" document of particular relevance; the considered to involve an inventive step				
	ent referring to an oral disclosure, use, exhibition or other	combined with one or more other such	documents, such			
"P" docume	means combination being obvious to a person skilled in the art document published prior to the international filing date but later "&" document member of the same patent family					
	e priority date claimed	Date of mailing of the international searce	ah ranart			
	une, 2003 (12.06.03)	24 June, 2003 (24.0				
			·			
Name and m	ailing address of the ISA/	Authorized officer				
	nese Patent Office					
Facility 3. 35		Tolonhous No.				
Facsimile No	0.	Telephone No.				

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP03/06054

Box 1	Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This	nternational search report has not been established in respect of certain claims under Article 17(2)(a) for t	he following reasons:
1. [Claims Nos.: 26 to 33	
	because they relate to subject matter not required to be searched by this Authority, namely: Inventions according to said claims relate to subject matter be searched by this Authority in accordance with PCT Artic PCT Rule 39.1. (see extra sheet for details)	
2. 「	Claims Nos.:	
_	because they relate to parts of the international application that do not comply with the prescribed requestent that no meaningful international search can be carried out, specifically:	uirements to such an
3. [Claims Nos.:	
	because they are dependent claims and are not drafted in accordance with the second and third senten	ces of Rule 6.4(a).
Box	Observations where unity of invention is lacking (Continuation of item 3 of first sheet)	
This	nternational Searching Authority found multiple inventions in this international application, as follows:	
	·	
1.	As all required additional search fees were timely paid by the applicant, this international search report	rt covers all searchable
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority d of any additional fee.	id not invite payment
3.	As only some of the required additional search fees were timely paid by the applicant, this internation only those claims for which fees were paid, specifically claims Nos.:	al search report covers
	•	
4. [No required additional search fees were timely paid by the applicant. Consequently, this international restricted to the invention first mentioned in the claims; it is covered by claims Nos.:	search report is
Dom	The additional course from user account to the applicant's protect	
Kem	The additional search fees were accompanied by the applicant's protest.	
	No protest accompanied the payment of additional search fees.	

INTERNATIONAL SEARCH REPORT

International application No. PCT/JP03/06054

Continuation of Box No.I-1 of continuation of first sheet(1)

"Method for drug design" according to the present invention relates to the design of a compound to be bonded to a protein, on the basis of the information on the three-dimensional structure of the protein. The design according to the present invention involves the work of the inventor to estimate a suitable compound by his mental acts, and such work is considered to correspond to the performance of purely mental acts.
constacted to correspond to the performance of parent member access
·
<u>.</u>

	属する分野の分類(国際特許分類(IPC)) 2N9/12, C12Q1/48			
			•	
	行った分野			
	最小限資料(国際特許分類(IPC)) 2N9/12, C12Q1/48			
	,,			
E I BELVirolal or	Li Shahi agarah San			
最小限資料以為	外の資料で調査を行った分野に含まれるもの			
国際調査で使	用した電子データベース (データベースの名称、	調査に使用した用語)		
1	OSIS(DIALOG), WPI(DIALOG) PIR/Genbank/EMBL/DDBJ/GeneSeq			
	ると認められる文献			
引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連する。	ときは、その関連する箇所の表示	関連する 請求の範囲の番号	
<u>X</u> A	TANIZAWA Y. Tanizawa, et al., Hum	nan Liver Glucokinase Gene:	1	
A	Cloning and Sequence Determination	on of Two Alternatively	2-25	
	Spliced cDNAs Proc. Natl. Acad. Sci. USA., 1991, Vo	ol. 88. n. 7294–7297		
	,	, p. 1301 (20)		
l A	MAHALINGAM B. et al., Structural	model of human alucokinaso	1-25	
	in complex with glucose and ATP.	_	1 25	
	Diabetes, 1999, Vol. 48, p1698-170)5		
区欄の続き	きにも文献が列挙されている。	□ パテントファミリーに関する別	紙を参照。	
* 引用文献(の日の後に公表された文献		
もの	車のある文献ではなく、一般的技術水準を示す	「T」国際出願日又は優先日後に公表さ 出願と矛盾するものではなく、多		
	頭日前の出願または特許であるが、国際出願日 公表されたもの	の理解のために引用するもの「X」特に関連のある文献であって、	48なか赤4の7、一次82日	
「L」優先権主	主張に疑義を提起する文献又は他の文献の発行	の新規性又は進歩性がないと考え	とられるもの	
文献(現	くは他の特別な理由を確立するために引用する 里由を付す)	「Y」特に関連のある文献であって、当 上の文献との、当業者にとって自		
「O」口頭による開示、使用、展示等に官及する文献 よって進歩性がないと考えられるもの 「P」国際出願日前で、かつ優先権の主張の基礎となる出願 「&」同一パテントファミリー文献				
国際調査を完了	12.06.03	国際調査報告の発送日 24.05.03	الله الله	
	の名称及びあて先	特許庁審査官 (権限のある職員)	4B 3037	
	国特許庁 (ISA/JP) 郵便番号100-8915	鈴木 恵理子 印		
	第千代田区霞が関三丁目4番3号	電話番号 03-3581-1101	内線 3488	

C (続き) .	関連すると認められる文献	
引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
A	WILLSON M. et al., Yeast hexokinase inhibitors designed from the 3-D enzyme structure reboilding. J. Enzyme Inhib., 1997, Vol. 12, No. 2, p. 101-121	1-25
·		
	·	

請求の範囲の一部の調査ができないときの意見(第1ページの2の続き) 等3項(PCT17条(2)(a))の規定により、この国際調査報告は次の理由により請求の範囲の一部について作いった。
請求の範囲 <u>26-33</u> は、この国際調査機関が調査をすることを要しない対象に係るものである。 つまり、
当該請求の範囲に記載された発明は、PCT17条(2)(a)(i)及びPCT規則39.1 (i i i) の規定により、この国際調査機関が調査することを要しない対象に係るものである。 (詳細は「特別ページ」を参照されたい)
請求の範囲 は、有意義な国際調査をすることができる程度まで所定の要件を満たしていない国際出願の部分に係るものである。つまり、
請求の範囲 は、従属請求の範囲であってPCT規則6.4(a)の第2文及び第3文の規定に 従って記載されていない。
発明の単一性が欠如しているときの意見(第1ページの3の続き)
☆べるようにこの国際出願に二以上の発明があるとこの国際調査機関は認めた。
出願人が必要な追加調査手数料をすべて期間内に納付したので、この国際調査報告は、すべての調査可能な請求 の範囲について作成した。
追加調査手数料を要求するまでもなく、すべての調査可能な請求の範囲について調査することができたので、追加調査手数料の納付を求めなかった。
出願人が必要な追加調査手数料を一部のみしか期間内に納付しなかったので、この国際調査報告は、手数料の納付のあった次の請求の範囲のみについて作成した。
出願人が必要な追加調査手数料を期間内に納付しなかったので、この国際調査報告は、請求の範囲の最初に記載されている発明に係る次の請求の範囲について作成した。

『第1ページの続葉(1)「第1欄1.」』の続き

本願発明に係る「ドラッグデザイン方法」は、タンパク質の立体構造情報に基づいて該タンパク質に結合する化合物の構造をデザインすることであるが、発明者がその精神活動によって適切な化合物を推測する行為を包含しており、これは純粋に精神的な行為の遂行に相当すると認められる。

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Specification

Crystal of glucokinase protein and drug design method using crystal thereof.

The Field of Technology

This invention relates to crystal of novel glucokinase protein (hereinafter it is called "GK protein") and the drug design method or the like employing three-dimensional structure coordinates obtained by using

the crystal thereof.

Background Technique

Glucokinase (ATP: D-hexose 6-phosphotransferaze, EC2.7.1.1) is one of four kinds of hexokinase isozymes of mammals (hexokinase IV). These isozymes catalyse the same reaction, however, differences exist in the Km value with respect to glucose. In other words, the Km value of hexokinase I, II and III being 10^{-6} - 10^{-4} M, but on the other hand the Km value of hexokinase IV, called glucokinase with respect

to glucose is much greater at about 10⁻² M. Hexokinase is an enzyme participating in the initial stage of

glycolytic pathway, and catalyses the reaction from the glucose to glucose-6-phosphate.

As for glucokinase, the expression is mainly localised in liver and pancreatic beta cell, and it plays an important role in glucose metabolism of the whole body by controlling the rate-determining step of glucose metabolism in these cells. As for the glucokinase of liver and pancreatic beta cell, the sequence of 15 amino acids at N terminal is respectively different due to splicing difference. However, the enzymatic

characteristics are the same.

The hypothesis that glucokinase acts as glucose sensor of pancreatic beta cell and liver is proposed since approximately 10 years ago (Garfinkel D, et al: Am J Physiol 247 [3Pt2]: R527-536, 1984). In practice, it is becoming clear from results of recent glucokinase gene manipulation mouse, that the glucokinase

plays an important role in glucose homeostasis of the whole body.

The mouse in which glucokinase gene is destroyed dies of diabetes mellitus soon after birth (Grupe A, et al: Cell 83: 69-78. 1995). On the other hand, as for the mouse which overexpressed glucokinase, the blood glucose level becomes low (Ferre T, et al: Proc Natl Acad Sci USA 93: 7225-7230. 1996). When

glucokinase activity is increased by the rise in glucose concentration, although the reactions of

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pancreatic beta cell and hepatocyte are different, in each case, it acts in the direction of lowering blood glucose. The pancreatic beta cell starts to secrete more insulin, the liver takes up sugar and stores as glycogen and at the same time lowers the sugar release.

In this way, the fluctuation of glucokinase enzyme activity plays an important role in glucose homeostasis of mammal through liver and pancreatic beta cell. Glucokinase gene mutation is discovered in the case that develops diabetes mellitus in youth known as MODY2 (maturity-onset diabetes of the young), and the lowering of glucokinase activity is said to be the cause of blood glucose rise (Vionnet N, et al.: Nature 356: 721-722, 1992). On the other hand, the lineage having mutation to increase glucokinase activity is also found, and such persons show hypoglycemic symptom (Glaser B, et al.: N Engl J Med 338: 226-230, 1998).

From the above, glucokinase also acts glucose sensor in human and plays an important role in glucose homeostasis. On the other hand, because the glucokinase of many type II diabetics is not mutated, the blood glucose control using glucokinase sensor system is considered possible. Because the glucokinase activator substance can be expected to have insulin secretion promotion action of pancreatic beta cell and sugar up take acceleration and sugar release suppression actions in liver, it is considered as useful therapeutic drug of type II diabetic patients.

Recently, a localised expression of pancreatic beta cell type glucokinase was found in rat brain, in particular in ventromedial hypothalamic nucleus (Ventromedial hypothalamus, VMH) which is the feeding centre. About 20 % of neurons of VMH was known as glucose responsive neuron, and it has been considered to play an important role in weight control in the past. When glucose is administered intracerebrally to rat, food consumption falls, whereas when the glucose metabolism is suppressed by administration of glucose analogue, glucosamine in brain, overeating occurs. From electrophysiological experiment, glucose responsive neurons are found to be activated in response to physiological glucose concentration changes (5-20 mM), however its activity is suppressed when the glucose metabolism is inhibited with glucosamine and the like. In glucose concentration sensing system of VMH, a mechanism through glucokinase the same as insulin secretion of pancreatic beta cells is assumed. Accordingly, there is a possibility that a substance that causes glucokinase activation of VHM in addition to liver, pancreatic beta cell is expected to correct problem of obesity which is a problem in many type II diabetic patients,

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in addition to blood glucose correction effect.

On the other hand, it is described in DIABETES, vol. 48, 1698-170, September 1999 that the stereostructure of glucokinase was predicted from hexokinase 1. However, in practice, crystallisation was not carried out, nor it was a practical one.

In accordance with the above, to elucidate three-dimensional stereostructure of glucokinase and to enable efficient discovery of a compound that interacts with glucokinase are thought to greatly contribute to the development of for example a therapeutic agent or preventative agent of diabetes, a therapeutic agent or preventative agent of chronic complication of diabetes mellitus such as retinopathy, nephropathy, neurosis, ischemic cardiac disease, arteriosclerosis or the like, a therapeutic agent or preventative agent of obesity.

Presently, CARDD (Computer Aided Rational Drug Design) using computer for the tasks such as analysis of active centre of a protein or a prediction of reaction mechanism has been employed at practical level.

In the drug creation system using CARDD, the structure of active site of plotein is predicted based on the three-dimensional structure analysis data of the target protein. And information about candidate compounds which can bind to the structure of active site thereof is btained from the compound database. Thereafter, on consideration of the three-dimensional structure and physical properties of the active site of the target protein and the candidate compound, candidate compounds which can bind to the target protein are selected. These steps are so-called in silico screening ster.

Whether the compound selected by in silico screening step binds to the arget protein and change the activity thereof or not, is examined by actual examination (wet experiment). And the compound that changes the activity of the target protein becomes the effective ingedient of a drug. Thereby a compound that interacts with the target protein can be efficiently scre ned without carrying out the procedure wherein innumerable compounds are acted on the target ; rotein one by one and the interactions are confirmed.

In silico screening can be said as an effective means of pharmaceut al development because the

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candidate compounds that bind to the target protein can be greatly narrowed down.

Three-dimensional structure analysis data by X-ray structure analysis of the target protein becomes an important information in drug creation system using CARDD. Crystal of target protein is required as analysis sample in three-dimensional structural analysis by X-ray structure analysis. Accordingly, in order to carry out development of drug creation related to GK based on the drug creation system using

CARDD, the crystal of GK is required. However, as stated above, crystallisation of GK was difficult, and

it could not provide information necessary for CARDD.

This invention was made on consideration of the problems of aforesaid technology of the prior art, and

had objects to obtain crystal of glucokinase and to design compounds that bind to glucokinase based on

the information obtained from aforesaid crystal.

Disclosure of the Invention

At least one of aforesaid objects is solved by the following invention.

[1] A glucokinase protein characterised in being used for crystallisation.

[2] A protein in accordance with aforesaid [1] comprising amino acid sequence in accordance with

Sequence Number 5.

[3] A crystal of protein comprising amino acid sequence in accordance with Sequence Number 5 or amino

acid sequence substantially the same amino acid sequence thereof.

[4] A crystal in accordance with aforesaid [3], wherein the said protein is glucokinase protein.

[5] A crystal in accordance with aforesaid [3] comprising crystals of protein containing amino acid

sequence in accordance with Sequence Number 5.

[6] A crystal in accordance with aforesaid [3], wherein the lattice constant satisfies the following

equations (1)-(4)

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$$a = b = 79.9 + /-4 \text{ Å}$$
 (1)

$$c = 322.2 + / - 15 \text{ Å}$$
 (2)

$$alpha = beta = 90^{\circ}$$
 (3)

$$gamma = 120^{\circ} \tag{4}$$

- [7] A crystal in accordance with aforesaid [6], wherein the space group is P6₅22.
- [8] A crystal of protein specified by three-dimensional structure coordinates data in accordance with Table 1.
- [9] A crystal wherein in three-dimensional structure coordinates data changed in at least one data of three-dimensional structure coordinates data in accordance with Table 1, the mean square error between atoms of main chain of amino acid represented by three-dimensional structure coordinates data in accordance with Table 1 (C alpha atom) and C alpha atoms represented by the said changed three-dimensional structure coordinates data corresponding to aforesaid C alpha atoms is 0.6 Å or less.
- [10] A crystal in accordance with any of [3]-[9], wherein the compound binding site is constructed by at least one of amino acid residues of tyrosine 61 serine 69, glutamic acid 96 glutamine 98, isoleucine 159, methionine 210 tyrosine 215, histidine 218 glutamic acid 221, methionine 235, arginine 250, leucine 451 lysine 459 in amino acid sequence shown in sequence Number 5.
- [11] A crystal including a complex of the protein comprising amino acid sequence in accordance with Sequence Number 5 or amino acid sequence substantially the same amino acid sequence thereof and a compound which can bind to the said protein.
- [12] A crystal in accordance with aforesaid [11], wherein aforesaid compound is represented by formula (1).

[wherein, R1 shows halogen atom, -S-(O)p-A, -S-(O)q-B or -O-B (wherein, p and q are the same or different and denote an integer of 0-2, A denotes C1-C6 alkyl group of optionally substituted straight chain, B denotes optionally substituted five-membered or six-membered ring aryl group or heteroaryl group, R2 denotes a hydrogen atom or halogen atom, and

denotes an optionally substituted monocyclic or bicyclic heteroaryl group having a nitrogen atom adjacent to the carbon atom bonded to amide group].

[13]. A crystal in accordance with aforesaid [12], wherein aforesaid compound is any of the compound represented by formula (IIIa)-(IIIc).

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$$0 = \stackrel{CH_3}{\stackrel{}{\stackrel{}{=}} 0} 0 \qquad 0 \qquad \stackrel{S}{\stackrel{}{\stackrel{}{\stackrel{}{=}} 0}} CH_3$$

$$0 + \stackrel{CH_3}{\stackrel{}{\stackrel{}{\stackrel{}{=}} 0}} 0 \qquad 0 \qquad \stackrel{CH_3}{\stackrel{}{\stackrel{}{=}} 0} \qquad (IIIc)$$

[14] A protein in accordance with aforesaid [1] comprising amino acid sequence in accordance with Sequence Number 8.

[15] A crystal of protein comprising amino acid sequence in accordance with Sequence Number 8 or amino acid sequence substantially the same amino acid sequence thereof.

[16] A crystal in accordance with aforesaid [15], wherein the said protein is glucokinase protein.

[17] A crystal in accordance with aforesaid [15] comprising crystals of protein containing amino acid sequence in accordance with Sequence Number 8.

[18] A crystal in accordance with aforesaid [15], wherein the lattice constant satisfies the following equations

$$a = b = 103.2 + /-5 \text{ Å}$$
 (5)

$$c = 281.0 + / - 7 \text{ Å}$$
 (6)

$$alpha = beta = 90^{\circ}$$
 (7)

$$gamma = 120^{\circ}$$
 (8)

[19] A crystal in accordance with aforesaid [18], wherein the space group is P6₅22.

[20] A crystal of protein specified by three-dimensional structure coordinates data in accordance with Table 2.

[21] A crystal wherein in three-dimensional structure coordinates data changed at least one data of three-dimensional structure coordinates data in accordance with Table 2, the mean square error between atoms

of main chain of amino acid represented by three-dimensional structure coordinates data in accordance with Table 2 (C alpha atom) and C alpha atoms represented by the said changed three-dimensional structure coordinates data corresponding to aforesaid C alpha atoms is 0.6 Å or less.

[22] A process for the production of crystal containing a complex of protein and a compound that binds to the protein thereof, including

a protein production step wherein a protein containing the amino acid sequence having deletion of 1-50 amino acid residues from either or both of N terminal and C terminal of the protein containing amino acid sequence in accordance with Sequence Number 2 is produced, and

a protein reaction step wherein a compound that binds to the protein obtained in the said protein production step and the protein obtained in the said protein production step are reacted.

[23] A process to produce crystal of the kind wherein a crystal of a protein is produced, characterised in that a protein including amino acid sequence in accordance with Sequence Number 5 or amino acid sequence substantially the same amino acid sequence thereof and having glucokinase activity and a compound which can bind to the said protein are used.

[24] A process for the production of crystalline protein in accordance with aforesaid [23], wherein the compound which can bind to said protein is a compound represented by formula (1).

(1)

[wherein, R1 shows halogen atom, -S-(O)p-A, -S-(O)q-B or -O-B (wherein, p and q are the same or different and denote an integer of 0-2, A denotes C1-C6 alkyl group of optionally substituted straight chain, B denotes optionally substituted five-membered or six-membered ring aryl group or heteroaryl group, R2 denotes a hydrogen atom or halogen atom, and



denotes an optionally substituted monocyclic or bicyclic heteroaryl group containing nitrogen atom adjacent to the carbon atom bonded to amide group].

[25]. A process for the production of crystal in accordance with aforesaid [23] or [24] using co-crystallisation or soaking method

[26] A drug design method of the kind wherein based on stereostructural information of a protein, the structure of compound that binds to said protein is designed, characterised in that the stereostructure information of said protein is the information obtained by analysing crystal in accordance with any one of aforesaid [3]-[13] or [15]-[21].

[27] A drug design method in accordance with aforesaid [26] characterised in that

- a binding site deduction step wherein the compound binding site of said protein is deduced based on aforesaid stereostructure information, and
- a selection step wherein a compound compatible to the compound binding site deduced in aforesaid binding site deduction step is selected from compound library, are included.

[28] A drug design method in accordance with aforesaid [26] characterised in that

- a binding site deduction step wherein the compound binding site of said protein is deduced based on aforesaid stereostructure information, and
- a compound structure assembly step wherein the structure of compound compatible to compound binding site deduced in aforesaid binding site deduction step is constructed, are included.
- [29] A drug design method in accordance with aforesaid [26] characterised in that

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a binding site deduction step wherein the compound binding site of said protein is deduced based on

aforesaid stereostructure information, and

a design step wherein the structure of compound is designed by visual observation so that the compound

binding site deduced in aforesaid binding site deduction step and a compound compatible to said

compound binding site interact,

are included.

[30] A drug design method in accordance with any of aforesaid [26]-[29], wherein aforesaid compound

binding site is constituted by at least one of amino acid residue of tyrosine 61 - serine 69, glutamic acid

96 - glutamine 98, isoleucine 159, methionine 210 - tyrosine 215, histidine 218 - glutamic acid 221,

methionine 235, arginine 250, leucine 451 - lysine 459 in amino acid sequence shown in sequence

Number 5.

[31] A drug design method in accordance with any of aforesaid [26]-[30] further including a step to

measure physiological activity of the candidate compound predicted to be compatible to aforesaid

compound binding site.

[32] A drug design method in accordance with any of aforesaid [26]-[30] further including a binding

determination step wherein the candidate compound predicted to be compatible to aforesaid compound

binding site and a protein including amino acid sequence in accordance with and Sequence Number 5 or

amino acid sequence which is substantially the same amino acid sequence thereof are contacted, and

whether the candidate compound binds to the said protein or not is assessed.

[33] A process for the production of compound array including the compound group selected by drug

design method in accordance with any of aforesaid [26]-[30] is combined as compound array.

Brief Description of the Figures

Figure 1 is a ribbon diagram showing three-dimensional structure of glucokinase.

(Figure 1a is a ribbon diagram showing the structure of glucokinase (Δ1-11)/glucose/compound 1

(compound of formula IIIa). Moreover, the figure on the right is a rotated figure of the figure on the

left.)

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(Figure 1b is a ribbon diagram showing the simple substance of glucokinase [ΔI -15]. Moreover, the figure

on the right is a rotated figure of the figure on the left.)

Figure 2 is a figure showing coupling scheme of compound 1 (compound of formula IIIa) with respect to

the binding site of glucokinase ($\Delta I-11$)

Figure 3 is a figure showing the structure of binding site of glucokinase (ΔI -11).

Ideal form for Carrying Out the Invention

In this specification, amino acids, peptides and proteins are represented using abbreviations adopted from

the IUPAC-IUB biochemistry designation committee (CBN) shown below. Moreover, the sequence of

amino acid residues of peptide and protein are represented so that the N terminal to C terminal

comprises from the left end to the right end and moreover the N terminal comprises the first.

Hereinafter, each embodiment of this invention is described in greater detail.

(Glucokinase protein).

Firstly, this invention puts forward glucokinase protein characterised in being used for crystallisation.

Glucokinase protein (GK protein) is involved in extremely important sugar metabolism in vivo as

described above. Accordingly, by solving the three-dimensional structure of GK protein and by

elucidating active site of GK protein, it is possible to search compounds that bind to GK protein

(activator or inhibitor). Therefore it is important to clarify the three-dimensional structure of GK

protein.

As technique to clarify the three-dimensional structure of protein, X-ray crystal structure analysis is well

known. In other words, protein is crystallised, mono-chromatised X-ray is irradiated to the crystal

thereof, and three-dimensional structure of said protein is elucidated on the basis of the obtained X-ray

diffraction pattern (Blundell, T.L. and Johnson, L.N, PROTEIN CRYSTALLOGRAPHY, pp. 1-565,

(1976) Academic Press, New York). First GK protein needs to be crystallised in order to provide for the

x-ray crystal structure analysis of GK protein.

Wherein, the "GK protein" of this invention refers to human derived liver type glucokinase having amino acid sequence shown in sequence Number 2 and a protein containing amino acid sequence which is substantially the same as Sequence Number 2. Wherein, as aforesaid protein containing amino acid sequence which is substantially the same, a species having glucokinase activity is preferable. Accordingly, in this specification, the GK protein includes not only the human derived liver type glucokinase, however also human derived pancreas type glucokinase, and non-human derived GK proteins such as mouse, rat, monkey and the like. In this invention human liver type glucokinase is preferably used. In glucokinase derived from human, 15 amino acid residues at N terminal differ in the liver type and the pancreas type. Wherein, "glucokinase activity" refers to an activity to catalyse reaction from glucose to glucose-6-phosphate.

It is generally well known that the crystallisation of protein is difficult, and the GK protein was not able to be crystallised without treatment. These inventors carried out various investigations with trial and error, as a result succeeded in crystallisation of GK protein for the first time by deletion of 11 or 15 amino acids at the N terminal side of GK protein. It was thought that the deleted region protruded from the globular GK protein molecule when the crystallisation was attempted, as a result, caused steric hindrance between adjacent GK protein molecules, and prevented the crystallisation of the GK protein. In other words, in this invention, the crystal of GK protein was obtained by using a GK protein in which 11 amino acid residues at N terminal side is deleted (Sequence Number 5) or a GK protein in which 15 amino acid residues at N terminal side is deleted (Sequence Number 8) in the glucokinase in which amino acids sequence had been known however the crystallisation had been unsuccessful. Wherein the number of amino acids is not restricted as long as it is within a range that the steric hindrance disappears between adjacent crystals. In an embodiment for example, in amino acid sequence represented by Sequence Number 2, amino acids sequence or the like in which amino acid residues of 1-50, preferably 3-30, more preferably 5-25, more preferably still 8-18, most preferably 11-15 at N terminal side are deleted, can be used in this invention. Moreover, the amino acid sequence or the like in which amino acid residues of 1-8, preferably 1-7, more preferably 2-6 at C terminal side are deleted, is used in this invention.

(Crystal of glucokinase protein and a process for the production thereof).

Next, in this invention, crystals including protein containing amino acids sequence in accordance with Sequence Number 5, and Sequence Number 8 or amino acids sequence which is substantially the same as

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amino acid sequence thereof are put forward.

As described earlier, as GK protein used in crystallisation, proteins containing amino acids sequence in accordance with Sequence Number 5, and/or Sequence Number 8 or amino acids sequence which is substantially the same as amino acid sequence thereof, or the like are used.

The proteins containing amino acids sequence in accordance with Sequence Number 5, and/or Sequence Number 8 or amino acids sequence which is substantially the same as the amino acid sequence thereof (hereinafter it may be abbreviated as "GK protein" together with proteins containing amino acids sequence in accordance with Sequence Number 2 or amino acids sequence which is substantially the same as the amino acid sequence thereof) can be any as long as crystallisation is possible, and the amino acid sequence thereof is not restricted in particular. Wherein, the proteins containing amino acids sequence which is substantially the same as the amino acid sequence in accordance with Sequence Number 5, and/or Sequence Number 8 does not necessarily have glucokinase activity, and may be an inactive mutant (for example, a mutant inactivated by the presence of mutation at ATP binding site) as long as it has a crystal structure from which the information necessary for drug design can be obtained. Wherein, as proteins containing amino acids sequence which is substantially the same as the amino acid sequence in accordance with Sequence Number 2 or Sequence Number 5, amino acids sequences having about 60 % or more, preferably about 70% or more, more preferably about 80% or more, in particular preferably about 90% or more, and most preferably about 95% or more homology to the amino acids sequence in accordance with Sequence Number 2 or Sequence Number 5, or the like are nominated. Moreover, as proteins containing amino acids sequence which is substantially the same as the amino acids sequence in accordance with Sequence Number 2 or Sequence Number 5, for example, amino acids sequences in which amino acid residues of 1-10, preferably 1-5, more preferably 1-3 more preferably still 1-2 are substituted, deleted, added and/or inserted in the amino acids sequence in accordance with Sequence Number 2 or Sequence Number 5 are exemplified.

Three-dimensional structural analysis of GK protein is carried out for example as follows. Firstly, the protein is purified. And a series of steps such as crystallisation, X-ray diffraction intensity data collection, phase determination of each diffraction spot, electron density calculation, molecular model construction, refinement of structure or the like is carried out. As main equipment for performing

protein structure analysis, incubator for crystallisation, binocular microscope, X-ray diffractometer, three dimensional computer graphics apparatus or the like are used. The actual experimental process to produce protein crystals is divided into step to purify protein in large amount (several mg or more is preferred), a step to widely search conditions for obtaining crystal and a step to obtain high quality crystal suitable for X-ray analysis. Hereinafter, each step is described in concrete terms.

For crystallisation, GK protein is purified to high purity. As process for purification, well known processes can be used, and for example, column chromatography, salt precipitation, centrifugation or the like are used.

Purified GK protein is crystallised and provided as a sample for X-ray crystal structure analysis. Crystallisation is performed based on well known method such as vapor diffusion method, dialysis or the like. When obtaining protein crystals, many elements such as purity / concentration of protein, temperature, pH, concentration of the precipitant used need to be examined. Investigation of crystallisation conditions can be carried out over a wide range using commercial screening reagent, and it is preferably screened using 1-2 μ l of protein solution in protein concentration of 1-2 % per condition. In this way when microcrystals or the like are obtained, it is preferred to further refined the conditions.

Moreover, extremely many conditions must be searched in order to obtain crystal of GK protein. Accordingly, a large quantity expression system of the protein is preferably constructed also for the investigation of crystallisation condition. Generally, among proteins, many of the crystallising species are monodispersed in solution state, and polydispersed species do not crystallise in most cases. Therefore, N terminal of GK protein is successively removed, monodispersion properties of protein solution are assessed for the obtained protein using light scattering apparatus, and whether sample is suitable for crystallisation or not may be examined.

Next, using the obtained crystal of GK protein, X-ray diffraction intensity measurement is carried out. Recently, a method wherein the crystal is scooped with a ring of narrow thread or the like, is rapidly cooled to liquid nitrogen temperature, and is measured at low temperature as it is, may also be used. Usually, the intensity measurement of diffracted x-ray is performed by two-dimensional detector such as image plate or the like. Many diffraction lines generated by rotating crystal while irradiating the X-ray

are recorded on image plate, and the recorded diffraction intensities are read by shining a laser.

Next, it is preferred to prepare heavy atom iso-form replacement bodies by heavy atom soaking method or co-crystallisation method. Using this, the phase of the protein crystal can be determined by multiple isomorphous replacement method (MIR method). Instead of introducing heavy atom, the phase is also determined by multiwavelength anomalous scattering method (MAD method) based on the diffraction intensity data using complex X-rays. Molecular replacement method (MR method) in which, when a structure of molecule containing analogous structure has been already solved, the initial structure can be obtained by applying the molecular structure thereof in the crystal, Furrier synthesis diagram is drawn on the basis of this, and the structure of remaining part is elucidated, and the total structure is determined, is known as well.

Once the phase was determined by aforesaid process, electron density is determined from this. The precision of this depends on the number of reflection (resolution) and the precision of the reflection used. The resolution is expressed with the minimum plane spacing of the reflection used. Molecular model is constructed from this electron density diagram. When the molecular model is constructed, the atomic coordinates are obtained, therefore, the calculated value of structure factor is determined from this, and refinement of atomic parameters is carried out by the least-square method to approximate this size to the observed value. In this way, the most reasonable structural information is obtained.

In accordance with this invention, the crystal of GK protein shown in sequence Number 5 has been successfully prepared (cf. later described Example). The obtained crystal of GK protein had lattice constant which satisfied the following equations (1)-(4).

$$a = b = 79.9 + /-4 \text{ Å}$$
 (1)

$$c = 322.2 + /- 15 \text{ Å}$$
 (2)

$$alpha = beta = 90^{\circ}$$
 (3)

$$gamma = 120^{\circ}$$
 (4)

Moreover, this crystal was elucidated to have space group $P6_522$. Wherein, aforesaid a = b is preferably 79.9 + /- 3 Å, more preferably 79.9 + /- 2 Å and even more preferably 79.9 + /- 1 Å. Moreover, aforesaid c is preferably 322.2 + /- 10 Å, more preferably 322.2 + /- 8 Å, and even more preferably 322.2 + /- 5 Å.

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The three-dimensional structural coordinates of the GK protein crystal obtained in this way are shown in Table 1.

Table 1

Moreover, Table 1 is constructed in accordance with representation method of protein data bank generally used by a person skilled in the art. The GLC in Table 1 denotes glucose molecule, and CP1 denotes the compound represented by formula IIIa, and HOH denotes water molecule.

Moreover, in this invention, the crystal of GK protein shown in sequence Number 8 has been successfully prepared (cf. later described Example). The obtained crystal of GK protein had lattice constant which satisfied the following equations (5)-(8).

$$a = b = 103.2 + / - 5 \text{ Å}$$

$$c = 281.0 + / - 7 \text{ Å}$$
 (6)

(5)

$$alpha = beta = 90^{\circ}$$
 (7)

$$gamma = 120^{\circ}$$
 (8)

Moreover, this crystal was elucidated to have space group $P6_522$. Wherein, aforesaid a = b is preferably 103.2 + -3 Å, more preferably 103.2 + -2, and even more preferably 103.2 + 1 Å. Moreover, aforesaid c is preferably 281.0 + -6 Å, more preferably 281.0 + 4 Å, and even more preferably 281.0 + 2 Å.

The three-dimensional structural coordinates of the GK protein crystal obtained in this way are shown in Table 2.

Table 2

Moreover, Table 2 is constructed in accordance with representation method of protein data bank generally used by a person skilled in the art. The HOH in Table 2 denotes water molecule.

In this invention, crystals of the protein having amino acids sequence which is substantially the same as Sequence Number 5 and/or Sequence Number 8 and having glucokinase activity are within the range of this invention. As such crystals, for example, crystals wherein in three-dimensional structure coordinates data changed at least one data of three-dimensional structure coordinates data in accordance with Table 1 and/or 2, the mean square error between atoms of main chain of amino acid represented by three-dimensional structure coordinates data in accordance with Table 1 and/or 2 (C alpha atom) and C alpha atoms represented by the said changed three-dimensional structure coordinates data corresponding to aforesaid C alpha atoms is 0.6 Å or less, are nominated. Even if the numerical values of coordinates representing the position of atoms differ, two structural coordinates which can superimpose corresponding atoms contained in the structural coordinates on top of one another show the same three-dimensional structure.

Moreover, the three-dimensional structural coordinates of GK protein in accordance with Table 1 and/or Table 2 are important information for drug design, and stored in a storage medium that can be read by computer in accordance with requirements, this information is processed with computer, and drug design is carried out. Accordingly, in another embodiment of this invention, a computer readable recording medium which recorded a program to function a computer as three dimensional coordinate memory means that memorises three-dimensional coordinates of amino acid residue in accordance with Table 1 and/or 2 is put forward.

Moreover, according to another embodiment of this invention, a computer readable recording medium that recorded a program which functions using computer as three dimensional coordinates memory means that memorised the three-dimensional coordinates of amino acid residue in accordance with Table 1 and/or 2, as binding site deduction means that deduces compound binding site of a protein having amino acid sequence represented by Sequence Number 8 and/or Sequence Number 5 using three dimensional coordinates of amino acid residue in accordance with Table 1 and/or 2 memorised in aforesaid three-dimensional coordinates memory measure, as binding compound memory means which memorised information about the type of compounds that bind to the protein and three-dimensional structure of aforesaid compounds, and as binding compound candidate selection means for selecting candidate compounds which are compatible to the compound binding site of the protein having amino acid sequence represented by Sequence Number 1 at least using the information about the three-dimensional structure of compound binding site of protein containing amino acid sequence represented by Sequence Number 5 deduced by aforesaid binding site deduction means and the

information about three-dimensional structure of compound memorised in aforesaid binding compounds memory means, is put forward. Moreover, according to another embodiment of this invention, a computer equipped with aforesaid each means, is also put forward.

(Crystal of complex of GK protein with compound that binds to this).

Next, according to another embodiment of this invention, a crystal containing a complex of protein including amino acid sequence in accordance with Sequence Number 5 or Sequence Number 8 or amino acid sequence which is substantially the same amino acid sequence thereof with the compound which can bind to the said protein and a process for the production thereof are put forward.

When a compound which binds to GK protein is obtained, firstly, the GK protein and the compound thereof are mixed for example in an aqueous solution, and a complex is formed. As for the crystal of such complex, well known processes for the production of co-crystals such as co-crystallisation, soaking method or the like are used. As for the crystallisation condition and crystallisation process, refer to aforesaid processes.

For example, a compound that binds to GK protein is selected from the compound group represented by aforesaid formula (I).

Wherein, as halogen atom of aforesaid formula (I), fluorine atom, chlorine atom, bromine atom, iodine atom or the like are exemplified, and among these, chlorine atom is preferred.

Moreover, as far as substituents in heteroaryl group of A, B of aforesaid formula (1) and formula (II) are concerned, amino group, carbamoyl group, cyclic C3-C6 hydrocarbon group, aralkyl group, N-aralkyl amino group, N,N-diaralkyl amino group, aralkyloxy group, aralkyl carbonyl group, N-aralkyl carbamoyl group, aryl group, arylthio group, N-arylamino group, aryloxy group, aryl sulphonyl group, aryl sulphonyloxy group, N-arylsulfonylamino group, aryl sulphamoyl group, N-aryl carbamoyl group, aroxy group, C2-C6 alkanoyl group, N-C2-C6 alkanoyl group, C1-C6 alkylthio group, C1-C6 alkyl sulphamoyl group, C1-C6 alkyl sulfinyl group, C1

C6 alkylsulfonyl group, N-C1-C6 alkylsulfonyl amino group, C1-C6 alkoxy group, C1-C6 alkoxycarbonyl group or C1-C6 alkylamino group are denoted), or the like is nominated. Wherein, as for the preferably used substituent, amino group, carbamoyl group, carbamoyl amino group, carbamoyloxy group, carboxyl group, cyano group, sulphamoyl group, trifluoromethyl group, halogen atom, hydroxy group, formyl group, straight chained C1-C6 alkyl group or the like are exemplified.

Wherein, "hydrocarbon group" denotes 1-6 C straight chained alkyl group, or, among carbon atom constituting said alkyl group, a group in which 1 or 2, preferably 1 carbon atom may be substituted with nitrogen atom, sulfur atom or oxygen atom and/or carbon atom themselves in the said 1-6 C straight chain alkyl group may be bonded with double bond or triple bond. Number of said double bond or triple bond is preferably 1 or 2 and 1 is more preferred.

As said hydrocarbon group, in an embodiment, it is preferred to be methyl group, ethyl group, propyl group or isopropyl group, butyl group or a group represented by following formulae

More preferred hydrocarbon group is methyl group, ethyl group, propyl group, isopropyl group or a group represented by following formulae

For example, as preferred A (in case of p = 0), the following groups are nominated.

As preferred B, for example, the following groups are nominated.

As heteroaryl group represented by formula (II), for example following heterocyclic groups are nominated.

Moreover, particularly preferred compounds are any of the compound represented by aforesaid formulae (IIIa)-(IIIc).

The compound of this invention (1) can be readily produced by using well known reaction means or according to well known method. Moreover, the compound of general formula (I) of this invention can be produced not only by synthesis in ordinary liquid phase, but also by synthesis using solid phase developed remarkably in recent years such as combinatorial synthesis method, parallel synthesis method or the like. Preferably, it can be produced for example using the following process.

Step 1 to Step 2 to Step 3

(wherein, each symbol is the same as in the aforesaid definition)

Step 1

This step is a process to produce compound (3) by reacting carboxylic acid compound (1) or reactive derivative thereof and amino compound containing optionally substituted monocyclic or bicyclic heteroaryl group represented by aforesaid formula (2) or salts thereof. In this reaction, ordinary amide formation reaction may be carried out by a method described in literature (for example Base and experiment of peptide synthesis, Shinya Izumiya et al., Maruzen, 1983, Comprehensive Organic Synthesis, vol 6, Pergamon Press Co. 1991 and the like) or in accordance with these, or by combining these and conventional method, in other word, it can be carried out by using condensing agent wellknown for a person skilled in the art or by ester activation method, mixed acid anhydride method, acid chloride method, carbodiimide method and the like which can be used by a person skilled in the art. As such amide forming reagent, for example thionyl chloride, N,N-dicyclohexylcarbodiimide, 1-methyl-2bromo pyridinium iodide, N,N'-carbonyldiimidazole, diphenyl phosphoryl chloride, diphenyl phosphoryl azide, N,N'-disuccinimidyl carbonate, N,N'-disuccinimidyl oxalato, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, ethylchloroformate, chloro formic acid isobutyl ester or benzo triazol-1-yloxy-tris (dimethylamino) phosphonium hexafluoro phosphate and the like are proposed, and wherein, example thionyl chloride, N,N-dicyclohexylcarbodiimide or benzo triazol-1-yl-oxy-tris (dimethylamino) phosphonium hexafluoro phosphate and the like are suitable. Moreover, in amide forming reaction, a base, a condensation assistant may be used with the aforesaid amide forming reagent.

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As base used, for example tertiary aliphatic amine such as trimethylamine, triethylamine, N,N-

diisopropyl ethylamine, N-methylmorpholine, N-methylpyrrolidine, N-methylpiperidine, N,N-

dimethylaniline, 1,8-diazabicyclo[5.4.0] undec-7-ene (DBU), 1,5-azabicyclo[4.3.0] non-5-ene (DBN) or

the like, for example aromatic amine such as pyridine, 4-dimethylaminopyridine, picoline, lutidine,

quinoline, isoquinoline and the like are proposed, and wherein, for example tertiary aliphatic amine and

the like is preferred, and in particular, for example triethylamine or N,N-diisopropyl ethylamine and the

like is suitable.

As condensation assistant used, for example N-hydroxybenzotriazole hydrate, N-hydroxy succinimide,

N-hydroxy-5-norbornene-2,3-dicarboximide or 3-hydroxy-3,4-dihydro-4-oxo-1,2,3-benzotriazole and

the like are proposed, and among these, for example N-hydroxybenzotriazole and the like are suitable.

The amount of amino compound (2) used differs depending on the kind of compound and solvent used

and other reaction conditions, however, usually, 0.02 to 50 equivalents, preferably 0.2 to 2 equivalents

with respect to 1 equivalent of carboxylic acid compound (1) or reactive derivative thereof. Herein, as

reactive derivative, for example active ester derivative, active amide derivative and the like which are

used in the sphere of usual organic chemistry are nominated.

The amount of used amide forming reagent differs depending on the kind of compound and solvent used

and other reaction conditions, however, usually 1-50 equivalents, preferably 1-5 equivalents with respect

to 1 equivalent of carboxylic acid compound (1) or reactive derivative thereof.

The amount of used condensation assistant differs depending on the kind of compound and solvent used

and other reaction conditions, however, usually it is 1-50 equivalents, preferably 1-5 equivalents with

respect to 1 equivalent of carboxylic acid compound (1) or reactive derivative thereof.

The amount of used base differs depending on the kind of compound and solvent used and other reaction

conditions, however, usually 1 to 50 equivalents, preferably 3 to 5 equivalents.

The reaction solvent used in this step, is for example insert organic solvent, and it is not restricted in

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particular so long as it does not hinder the reaction. However, in an embodiment, for example methylene

chloride, chloroform, 1,2-dichloroethane, trichloroethane, N,N-dimethylformamide, acetic acid

ethylester, acetic acid methylester, acetonitrile, benzene, xylene, toluene, 1,4-dioxane, tetrahydrofuran,

dimethoxyethane or a mixed solvent thereof are proposed, however, in particular for example

methylene chloride, chloroform, 1,2-dichloroethane, acetonitrile, N,N-dimethylformamide or the like

are suitable in term of securing a suitable reaction temperature.

The reaction temperature is -100°C to boiling point of solvent, preferably 0 to 30°C.

The reaction time is 0.5 to 96 hours, preferably 3 to 24 hours.

The base, amide formation reagent, condensation assistant used in this step 1 can be used as a single

species or in combination of two or more.

When the compound (3) contains protecting group, said protecting group can be suitably eliminated.

Elimination of aforesaid protecting group can be carried out by method described in literature (Protective

Groups in Organic Synthesis, written by T.W. Green, the second edition, John Wiley & Sons Co, 1991,

or the like) or method in accordance with this or by combining these and conventional method.

Compound (3) obtained in this way can be provided for the next step by isolating and purifying with well

known separation and refinement means, for example concentration, vacuum concentration,

crystallisation, solvent extraction, re-precipitation, chromatography and the like or without isolating

and purifying.

Step 2

This step comprises a process to produce compound (5) by reacting amide compound (3) obtained in

aforesaid step 1 and compound (4).

In this reaction, a base may be added to the reaction system in accordance with requirements. As used

compound (4), preferably phenol derivative or thiol derivative is preferred. As said phenol derivative or

thiol derivative, for example phenol, thiophenol, thio imidazole, thio triazole and the like are

nominated. The amount of compound (4) used differs depending on the kind of compound and solvent used or other reaction conditions, however, usually it is 2-50 equivalents, preferably 2-5 equivalents with respect to 1 equivalent of amino derivative (3). As used base, for example tertiary aliphatic amine such N,N-diisopropyl trimethylamine, triethylamine, ethylamine, N-methylmorpholine, methylpyrrolidine, N-methylpiperidine, N,N-dimethylaniline, 1,8-diazabicyclo[5.4.0] undec-7-ene (DBU), 1,5-azabicyclo[4.3.0] non-5-ene (DBN) or the like, for example aromatic amine such as pyridine, 4-dimethylaminopyridine, picoline, lutidine, quinoline, isoquinoline and the like, alkali metal such as metallic potassium, metallic sodium, metallic lithium and the like, alkali metal hydride such as sodium hydride, potassium hydride and the like, alkali metal alkylate such as butyl lithium and the like, alkali metal alkoxide such as potassium-tert-butyrate, sodium ethylate or sodium methylate and the like, alkali metal hydroxide such as potassium hydroxide, sodium hydroxide and the like, alkali metal carbonate such as potassium carbonate and the like are nominated, among these for example tertiary aliphatic amine, alkali metal hydride or alkali metal carbonate are preferred, and in particular, for example triethylamine, N,N-diisopropyl ethylamine, sodium hydride or potassium carbonate are suitable.

The amount of aforesaid base used differs depending on the kind of compound and solvent used and other reaction conditions, however, it is usually 0 to 50 equivalents, preferably 2-10 equivalents with respect to 1 equivalent of amide compound (3). Said base can be used as a single species or two or more species in accordance with requirements.

As used insert organic solvent, there are no restrictions in particular so long as the reaction is not hindered. However, in an embodiment, for example methylene chloride, chloroform, 1,2-dichloroethane, trichloroethane, N,N-dimethylformamide, N,N-dimethyl acetamide, acetic acid ethylester, acetic acid methylester, acetonitrile, benzene, xylene, water, toluene, 1,4-dioxane, tetrahydrofuran, or a mixed solvent thereof are proposed.

Compound (5) obtained in this way can be and isolated and purified with well known separation and refinement means, for example concentration, vacuum concentration, crystallisation, solvent extraction, re-precipitation, chromatography and the like.

Step 3

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This step is a process to produce compound (I) used in this invention by reduction of compound (5). As

for reductive reaction used in this step, well-known processes to a person skilled in the art are used. As

the reductive reaction used in this step, in an embodiment, for example (1) catalytic reduction method

using hydrogen, formic acid, ammonium formate, hydrazine hydrate and palladium, platinum, nickel

catalyst, (2) reduction method using hydrochloric acid, ammonium chloride and iron, (3) reduction

method using methanol and tin chloride are nominated.

The amount of reducing agent used in the aforesaid reductive reaction differs depending on the kind of

compound and solvent to be used and other reaction conditions, however, it is usually 1-50 equivalents,

preferably 2-20 equivalents with respect to 1 equivalent of compound (5).

The reaction solvent used is not restricted in particular so long as the reaction is not hindered. However,

for example halogenated hydrocarbons such as dichloromethane, chloroform and the like, ethers such as

diethyl ether, tert-butyl methyl ether, tetrahydrofuran and the like, amides such as N,N-

dimethylformamide, N,N-dimethylacetamide and the like, sulphoxides such as dimethylsulfoxide and the

like, nitriles such as acetonitrile and the like, an alcohol such as methanol, ethanol, propanol and the

like, aromatic hydrocarbons such as benzene, toluene, xylene and the like, water or mixed solvent

thereof can be used.

Reaction temperature and the reaction time are not restricted in particular. However, the reaction is

carried out for 1-20 hours approx. and preferably 1 to 5 hours approx. at a reaction temperature of -10

to 100°C approx. and preferably 0 to 50°C approx.

Compound (1) used in this invention obtained in this way can be provided for the next step by isolating

and purifying with well known separation and refinement means, for example concentration, vacuum

concentration, crystallisation, solvent extraction, re-precipitation, chromatography and the like or

without isolating and purifying.

Compound of aforesaid each step may contain protecting group on each substituent. Aforesaid

protecting group can be suitably eliminated in each step using well known method, method in accordance

with that or method combined these and the conventional method. As for the embodiment of

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elimination, suitable elimination reaction is possible depending on the kind of compound, reaction and other reaction conditions. However, it is considered the case in which each protecting group is eliminated individually and the case in which each protecting group is simultaneously eliminated and the like, and it can be suitably selected by a person skilled in the art. As aforesaid protecting group, for example protecting group of hydroxy group, protecting group of amino group, protecting group of carboxyl group, protecting group of aldehyde, protecting group of keto group and the like are nominated. Moreover, the order of elimination aforesaid protecting groups is not limited in particular.

As protecting group of hydroxy group, for example lower alkyl silyl group such as tert-butyldimethylsilyl group, tert-butyl diphenyl silyl group and the like, for example lower alkoxymethyl group such as methoxy methyl group, 2-methoxyethoxymethyl group and the like, for example aralkyl group such as benzyl group, p-methoxybenzyl group and the like, for example acyl group such as formyl group, acetyl group and the like are proposed, and among these, tert-butyldimethylsilyl group, acetyl group and the like are in particular preferred.

As protecting group of amino group, for example aralkyl group such as benzyl group, p-nitrobenzyl and the like, for example acyl group such as formyl group, acetyl group and the like, for example lower alkoxycarbonyl group such as ethoxycarbonyl group, tert-butoxycarbonyl group and the like, for example aralkyloxy carbonyl group such as benzyloxycarbonyl group, p-nitrobenzyl oxycarbonyl group and the like are proposed, and among these, nitrobenzyl group, tert-butoxy carbonyl group, benzyloxycarbonyl group and the like are particularly preferred.

As protecting group of carboxyl group, for example lower alkyl group such as methyl group, ethyl group, tert-butyl group and the like, for example aralkyl group such as benzyl group, p-methoxybenzyl group and the like are nominated, and among these, methyl group, ethyl group, tert-butyl group, benzyl group and the like are particularly preferred.

As protecting group of keto group, for example dimethyl ketal group, 1,3-dioxirane group, 1,3-dioxolane group, 1,3-dithiorane group and the like are proposed, and among these, dimethyl ketal group, 1,3-dioxolane group and the like are more preferred.

As protecting group of aldehyde group, for example, dimethylacetal group, 1,3-dioxirane group, 1,3-dioxolane group, 1,3-dithiorane group and the like are proposed, and among these, dimethylacetal group, 1,3-dioxolane group and the like are more preferred.

In the production of compound used in this invention, there is a case that the protecting group is introduced to functional group in order to proceed reaction with good efficiency. The introduction of these protecting groups can be suitably selected by a person skilled in the art, and elimination of aforesaid protecting groups can be carried out by a method described in aforesaid Protective Groups In Organic Synthesis and the like, a method in accordance with that or by combining that and conventional method. Moreover, the order of elimination of protecting groups can be suitably selected by a person skilled in the art.

Compound (1) obtained in this way can be subjected to the next step after isolating and purifying with well known separation and refinement means, for example concentration, vacuum concentration, crystallisation, solvent extraction, re-precipitation, chromatography and the like or without isolating and purifying.

Moreover, the compound used in this invention (I) can be also produced by the following step.

Step 4 to Step 5 to Step 6

(wherein, each symbol has same aforesaid definition).

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As far as the aforesaid Step 4, Step 5 and Step 6 are concerned, it can be carried out using the same

amount of reagent, reaction solvent, reaction temperature and other reaction conditions as in aforesaid

Step 1, Step 2 and Step 3.

When a protecting group is necessary for R2, it can be carried out by a person skilled in the art suitably

selecting a process from a method described in aforesaid Protective Groups In Organic Synthesis and the

like, a method in accordance with that or by combining that and conventional method.

Compounds (6) and (5') obtained in this way can be provided for the next step after isolating and

purifying with well known separation and refinement means, for example concentration, vacuum

concentration, crystallisation, re-precipitation, solvent extraction and the like or without isolating and

purifying.

Compound (1) used in this invention can be isolated and purified by well known separation and

refinement means, for example concentration, vacuum concentration, crystallisation, re-precipitation,

solvent extraction and the like.

In aforesaid step 1 to 6, the elimination of protecting groups differ depending on the kind of aforesaid

protecting group and stability of compound, however, it can be carried out by aforesaid method described

in Protective Groups in Organic Synthesis, written by T.W. Green, the second edition, John Wiley &

Sons Co, 1991, or the like or a method in accordance with this or by combining these and conventional

method. For example, it can be carried out by solvolysis using acid or base, chemical reduction using

hydrogenated metallic complex and the like or catalytic reductions using palladium carbon catalyst,

Raney nickel and the like.

The benzamide compound put forward by this invention can exist as pharmacologically acceptable salt.

Aforesaid salt can be produced in accordance with conventional methods. In an embodiment, when

aforesaid compound (1) contains basic group derived from for example amino group, pyridyl group

within the molecule, it can be converted to corresponding pharmacologically acceptable salt by treating

aforesaid compound with an acid.

As aforesaid acid addition salt, for example the acid addition salt of halide acid salt such as hydrochloride, hydrofluoric acid salt, hydrobromic acid salt, hydroiodic acid salt or the like, inorganic acid salt such as nitrate, perchlorate, sulfate, phosphate, carbonate or the like, lower alkyl sulfonate such as methanesulfonate, trifluoromethanesulfonate, ethanesulfonic acid salt or the like, aryl sulfonate such as benzensuplhonate, p-toluenesulfonate or the like, organic salt such as fumarate, succinate, citrate, tartrate, oxalate, maleate or the like and organic acid of amino acid or the like such as glutamic acid salt, aspartate or the like are nominated. Moreover, when the compound of this invention is containing acidic group in aforesaid group, for example when containing carboxyl groups, it can be converted to corresponding pharmacologically acceptable salt by treating aforesaid compound with a base. As aforesaid base addition salt, for example salt of alkali metal salt such as sodium, potassium and the like, alkaline earth metal salt such as calcium, magnesium and the like, organic base such as ammonium salt, guanidine, triethylamine, dicyclohexylamine and the like are nominated. Furthermore, the compound of this invention may exist as free compound or arbitrary hydrate or solventate of salts thereof.

In accordance with this invention, as explained in detail in the description of Examples, crystal of complex of GK protein containing amino acid sequence shown in Sequence Number 5 and compounds of aforesaid formula (IIIa)-formula (IIIc) are obtained. In GK protein shown in Sequence Number 5, it has been elucidated that compound binding site is constituted from the amino acid residue of tyrosine 61 - serine 69, glutamic acid 96 - glutamine 98, isoleucine 159, methionine 210 - tyrosine 215, histidine 218 - glutamic acid 221, methionine 235, arginine 250, leucine 451 - lysine 459 by analysing these crystal three - dimensional structure coordinates.

Moreover, according to another embodiment of this invention, a process for the production of crystal containing a complex of protein and a compound that binds to the protein, wherein a protein production step to produce a protein containing amino acids sequence in which prescribed number of amino acid residues at N terminal side and/or C terminal side are deleted as described above from the protein containing amino acid sequence in accordance with Sequence Number 2 and a step to cause reaction of a compound which binds to the protein obtained in aforesaid protein production step with the protein obtained in said protein production step are included, is put forward.

As protein to be produced in the aforesaid protein production step, the number thereof is not restricted as long as it is within a range that steric hindrance between adjacent GK proteins in the crystal is eliminated. In an embodiment, for example, in the amino acids sequence shown in Sequence Number 2, the amino acids sequences in which amino acid residues at N terminal side are deleted in numbers of 1-50, preferably 3-30, more preferably 5-25, still more preferably 8-18, even more preferably 11-15 or the like are nominated. Moreover, the amino acid sequences in which amino acid residues at C terminal side of 1-8, preferably 1-7, more preferably 2-6 or the like are deleted, are nominated.

(The drug design process using three-dimensional structural coordinate).

Three-dimensional structure of GK protein of this invention obtained as above provides important information for drug creation system using CARDD (Computer Aided Rational Drug Design). It is an important step of the target drug creation and development to elucidate the active center and allosteric site of this GK protein and to search for a compound which is compatible to said site, interacts with the GK protein and thereby activates to inhibits the GK protein.

In other words, according to another embodiment of this invention, a drug design process of the kind to design structure of compound that binds to said protein based on stereostructure information of protein, characterised in that the stereostructure information of said protein comprises information to be obtained by analysing the crystal obtained as described above, is put forward. As such drug design process, there are techniques to make drug design using energy calculation, activity prediction value analogous to this or pharmacophore and a technique to visually design drug using computer graphics technique.

As process by technique using energy calculation, activity prediction value analogous to this or pharmacophore, (1) a drug design process including a binding site deduction step to deduce compound binding site of said protein based on stereostructural information obtained as above and a selection step to select a compound compatible to the compound binding site deduced in aforesaid binding site deduction step from the compound library, (2) a drug design process including a binding site deduction step to deduce compound binding site of said protein based on aforesaid stereostructural information and a compound structure assembly step to construct a structure of compound compatible to the compound binding site deduced in aforesaid binding site deduction step, or the like are exemplified.

As process to deduce compound binding site of aforesaid protein, for example, a process wherein the ligand bonded site in the co-crystal of compound is identified by confirming with visual observation on display of computer, and in addition to that, a process wherein the site to which ligand is likely to bind is identified with respect to the protein crystal structure solved under the condition that ligand is not bound, are nominated. In any processes, well-known method and commercial computer soft wear can be used. In former process, for example, it is possible to use software such as Insight II (Accelrys Inc.), SYBYL (Tripos Inc.), MOE (Chemical Computing Group) or the like. On the other hand, For example, in latter process, well known technique such as Cavity search: an algorithm for the isolation and display of cavity-like binding regions, (Journal of Computer-Aided Molecular Design. 4(4): 337-54, 1990) or the like can be used, and it can be carried out using software such as SiteID (Tripos Inc.) or the like.

Once the binding site of compound in protein was able to be deduced, a compound which can be compatible to the deduced binding site is selected. As process to select this candidate compound, structural information of the compound is acquired from existing compound library, and bindable candidate compound is selected by comparing the structural information of compound in the library and structural information of the binding site deduced as above.

In a further embodiment, 1 or more residues of amino acid residues of amino acid sequence shown in Sequence Number 5 (tyrosine 61 - serine 69, glutamic acid 96 - glutamine 98, isoleucine 159, methionine 210 - tyrosine 215, histidine 218 - glutamic acid 221, methionine 235, arginine 250, leucine 451 - lysine 459) or pharmacophore of hydrogen bonding or hydrophobic properties or the like formed from the functional group of ligand in the complex, and also the protein surface produced from the protein structure or a structure in which the orientation of a part of the side chain thereof is modified, are used as search condition, and the conformation and orientation of each compound is systematically searched from the compound library, and whether the conditions are satisfied or not is judged and it is selected.

As an alternative process, while systematically searching the conformation and orientation of each compound from the compound library, the candidate compound is virtually docked with respect to the structure of ligand binding site constructed from the amino acid residues (tyrosine 61 - serine 69, glutamic acid 96 - glutamine 98, isoleucine 159, methionine 210 - tyrosine 215, histidine 218 - glutamic acid 221, methionine 235, arginine 250, leucine 451 - lysine 459) or a structure in which the orientation

of a part of the side chain thereof is modified, the species that formed interaction of close proximity of 4 Å or less with 1 or more residues of amino acid residues of amino acid sequence (tyrosine 61 - serine 69, glutamic acid 96 - glutamine 98, isoleucine 159, methionine 210 - tyrosine 215, histidine 218 - glutamic acid 221, methionine 235, arginine 250, leucine 451 - lysine 459) is selected, or selection is carried out using energy evaluation function.

On the other hand, the candidate compound can also be selected by designing a bindable compound based on the structural information of the binding site deduced as above. In a further embodiment, each atomic species and functional groups are connected so that interactions are possible with respect to the structure of ligand binding site constructed from the amino acid residues (tyrosine 61 - serine 69, glutamic acid 96 - glutamine 98, isoleucine 159, methionine 210 - tyrosine 215, histidine 218 - glutamic acid 221, methionine 235, arginine 250, leucine 451 - lysine 459) or a structure in which the orientation of a part of the side chain thereof is modified, and thereby a chemical structure is constructed. As this process, a process wherein chemical groups such as methyl, ethyl and the like are arranged in the active site and a compatible compound is searched, and a process wherein atoms are bonded at active site using a computer program.

Moreover, with the process by energy evaluation using computer, for example a process to determine the bond energy of a compound and GK protein using molecular force field calculation is nominated. The calculation thereof is applied to each compound in database, and candidate compounds which can form stable binding are selected from the library compound. With some computer programs, such as Ludi of Insight II, when three-dimensional structural coordinates of interacting amino acid residues in the protein molecule are input, candidate of bindable compounds are automatically selected and output, and it can be suitably used.

Moreover, as far as the drug design on the basis of three-dimensional structure of molecule is concerned, many literature are known including development of pharmaceutical Vol. 7 "molecular design" (Hirokawa Shoten). In an embodiment, first, using flexible ligand binding simulation software such as for example FlexiDock, FlexX or the like, a library of low molecular (molecular weight 1000 or less) compounds (for example about 150000 species) can be screened with computer. For chemical compounds in this library, three-dimensional structure is built using a program such as CONCORD or the

like, and compounds compatible to the active site can be selected.

On the other hand, as a process of visual drug design, a drug design process characterised in including a binding site deduction step to deduce compound binding site of said protein based on aforesaid stereostructural information and a design step wherein the structure of the compound is visually designed so that aforesaid compound binding site deduced in aforesaid binding site deduction step and a compound compatible to said compound binding site can interact, is nominated. For example, structure assembly or structure modification is carried out with respect to the structure of ligand binding site constructed from the amino acid residues (tyrosine 61 - serine 69, glutamic acid 96 - glutamine 98, isoleucine 159, methionine 210 - tyrosine 215, histidine 218 - glutamic acid 221, methionine 235, arginine 250, leucine 451 - lysine 459) or a structure in which the orientation of a part of the side chain thereof is modified, so that it can interact with 1 or 2 or more residues among these residues.

In an embodiment, with visual process, first, crystal structure of the complex of GK protein and a compound bound to this is displayed on a computer screen according to the obtained structural coordinates. And, while considering the chemical interaction, the binding possibilities of the compounds in the library and GK protein are successively examined on computer. Wherein, the chemical interactions to be considered are electrostatic interaction, hydrophobic interaction, hydrogen bonding, van der Waals interaction or the like. In other words, the structure in three dimensional space of said compound is generally considered whether a structure favourable for the interaction is formed or not, so that among the functional groups thereof, the groups likely to be negatively charged such as carboxyl group, nitro group, halogen group or the like interact with amino acid residues having positive charge such as lysine, arginine, histidine of GK protein, the groups likely to be positively charged such as amino group, imino group, guanidyl group or the like interact with amino acid residues having negative positive charge such as glutamic acid, aspartic acid of GK protein, hydrophobic functional groups such as aliphatic group and aromatic group interact with hydrophobic amino acid residues such as alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine, the groups which participate in hydrogen bond such as hydroxy group, amide group or the like can for hydrogen bonding with the main chain or side chain part of the GK protein, furthermore steric hindrance is not caused by the binding of said compound and GK protein, moreover, furthermore, the void part is filled so that the void part is eliminated as much as possible so that the van der Waals interaction is increased, or the like. In this way,

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the factors such as electrostatic interaction, hydrophobic interaction, van der Waals interaction,

hydrogen bond or the like are comprehensively considered visually on the computer screen, and finally,

whether the candidate compound can bind to the GK protein or not is determined.

As program for selecting compound candidate by visual observation in this way, simulation programs

such as Insight II and MOE or the like are exemplified. In order to generate promising candidate

compounds that interact with GK protein, the candidate compounds are contacted with GK protein, and

activity of GK protein is measured. In practice, the promising candidate compound is mixed with GK

protein, crystallised, and whether it is compatible or not is evaluated. Further, more desirable structure is

formed by modifying the compatible complex using organic synthesis.

Moreover, the visual technique and the technique that considers energy may be suitably combined, and

used. As such computer software, flexiDock (Tripos Inc.), FlexX (Tripos Inc.), SYBYL (Tripos Inc.),

Insight II (Accelrys Inc.), MOE (Chemical Computing Group Inc.) or the like are nominated.

Moreover, in accordance with this invention, the compounds selected by aforesaid drug design process

are synthesized, and these compound groups can be provided as compound array (compound library).

Because a large quantity of candidate compounds can be assayed at one time using a technique such as

high through-put screening or the like, the inhibitor or activator of glucokinase can be screened with

good efficiency.

(Compounds obtained by process of this invention and therapeutic agent including these)

The compounds designed by aforesaid drug design process have has ability to bind to glucokinase,

therefore they can be used as activators of glucokinase or glucokinase inhibitors. Moreover, the

therapeutic agent or medicinal composition containing such compound can be effectively used as

therapeutic agent of disease involving glucokinase activity (for example diabetes mellitus therapeutic

agent).

Aforesaid medicinal composition contains a compound that binds to glucokinase of this invention as

effective ingredient in pharmacologically effective dose thereof together with suitable pharmacologically

permitted support or diluent. As the pharmacologically acceptable support which can be used in aforesaid

medicinal composition (drug formulation), diluent such as filler, extender, binding agent, humectant, disintegrating agent, surface active agent, lubricant or the like which are conventionally used corresponding to the form of the formulation or excipient or the like are exemplified. These carriers can be suitably selected and used corresponding to administration unit form of the obtained formulation.

As administration unit form of medicinal composition of this invention, various forms can be selected according to therapeutic purpose, and, as representative examples thereof, solid administrative form such as tablet, pill, powder, powder agent, granule, encapsulated formulation or the like and liquid agent administrative form such as solution, suspending agent, emulsion, syrup, elixir or the like are included. Further these are classified into orally administered agent, agral drug, transnasal agent, vaginal agent, suppository, sublingual agent, ointment or the like according to administration route, and it can be formulated, molded and prepared each according to conventional process. For example, when it is formed to a tablet form, excipient such as lactose, lactose, refined sugar, sodium chloride, glucose, urea, starch, calcium carbonate, kaolin, crystalline cellulose, silicic acid, potassium phosphate or the like, binding agent such as water, ethanol, propanol, simple syrup, glucose syrup, starch solution, gelatin solution, carboxymethylcellulose, hydroxypropylcellulose, methylcellulose, polyvinylpyrrolidone or the like, disintegrating agent such as carboxymethylcellulose sodium, carboxymethylcellulose calcium, low degree of substitution hydroxypropylcellulose, dried starch, sodium alginate, agar powder, laminaran powder, sodium bicarbonate, calcium carbonate or the like, surface active agent such as polyoxyethylene sorbitan fatty acid ester species, lauryl sodium sulfate, stearic acid monoglyceride or the like, disintegration inhibitor such as refined sugar, stearin, cacao butter, hydrogenation oil or the like, absorption accelerating agent such as quaternary ammonium base, sodium lauryl sulfate or the like, humectant such as glycerol, starch or the like, adsorbent such as starch, lactose, kaolin, bentonite, colloidal silica or the like, lubricant or the like such as purified talc, stearate, boric acid powder, polyethyleneglycol or the like can be used. Further, the tablet can be formed into a tablet coated with ordinary agent coating in accordance with requirements, for example sugar coated tablet, gelatin encapsulation tablet, enteric coated tablet, film coatings tablet and moreover can be made into double layer tablet or multilayer tablet.

When a form of pill is formed, as formulation carrier, for example, excipient such as glucose, lactose, starch, cacao butter, hardened vegetable oil, kaolin, talc or the like, binding agent such as powdered gum

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arabic, tragacanth powder, gelatin, ethanol or the like, disintegrating agent or the like such as laminaran,

agar or the like can be used.

For encapsulated formulation, effective ingredient of this invention is mixed with the various

formulation carrier exemplified as above according to normal method, and it is prepared by being packed

into hard gelatin capsule, soft capsule or the like.

The liquid administration form for oral administration includes pharmacologically permitted solution,

emulsion, suspension, syrup, elixir or the like containing generally used inert diluent, for example water,

and furthermore, auxiliary such as wetting agent, emulsion, suspending agent or the like can be contained,

and these are prepared according to normal method.

For the preparation of liquid administrative form for aoral administration, for example, sterile aqueous

or non-aqueous solution, emulsion, suspension or the like, as diluent, for example water, ethanol,

propylene glycol, polyethyleneglycol, ethoxylation isostearyl alcohol, polyoxyisosteary alcohol,

polyoxyethylene sorbitan fatty acid ester and vegetable oil or the like such as olive oil or the like can be

used, and moreover, injectable organic ester species, for example, ethyl oleate or the like can be

formulated. Further, ordinary solubilser, buffer agent, wetting agent, emulsifier, suspending agent,

preservative, dispersant or the like can be added to these. Sterilisation can be carried out for example by

filtration operation through bacteria retaining filter, formulation of fungicide, irradiation treatment and

heat treatment or the like. Moreover, these can be prepared as sterile solid composition which can be

dissolved in sterile water or suitable sterilisable vehicle immediately before the use.

When forming into a form of suppository or vaginal administration, as formulation carrier, for example

polyethyleneglycol, cacao butter, higher alcohol, higher alcohol ester, gelatin and semi-synthetic

glyceride or the like can be used.

When forming into a form ointment such as paste, cream, gel or the like, as diluent, for example white

petrolatum, paraffin, glycerol, cellulose derivative, propylene glycol, polyethyleneglycol, silicon,

bentonite and vegetable oil or the like such as olive oil or the like can be used.

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A composition for transnasal or sublingual administration can be prepared according to conventional

method using standard excipient.

Moreover, in agent of this invention, colorant, preservative, flavor, flavor agent, sweetener or the like

or other pharmaceutical or the like can be contained in accordance with requirements.

The amount of the effective ingredient to be contained in the aforesaid drug formulation and dose

thereof are not restricted in particular, and it is suitably selected from a wide range corresponding to the

desired therapy effect, administration method, therapy period, age, sex of patient, other conditions or

the like. In general, the dose is about 0.01 mg - 1000 mg, preferably about 1 mg - 100 mg per 60 kg in

weight per day usually, and it can be administered once or divided into several times per day.

Sequence number of sequence table of this specification shows following sequence.

(Sequence number: 1).

Base sequence of DNA encoding human derived liver type glucokinase is shown.

(Sequence number: 2).

Amino acid sequence of human derived liver type glucokinase is shown.

(Sequence number: 3).

Amino acid sequence of human derived beta cell glucokinase is shown.

(Sequence number: 4).

Base sequence of DNA encoding the protein in which 11 amino acid residues at N terminal side of human

derived liver type glucokinase are deleted, is shown.

(Sequence number: 5).

Amino acid sequence of the protein in which 11 amino acid residues at N terminal side of human derived

liver type glucokinase are deleted, is shown.

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(Sequence number: 6).

Base sequence of primer-1 used in PCR reaction in the following Example 1 is shown.

(Sequence number: 7).

Base sequence of primer-2 used in PCR reaction in the following Example 1 is shown.

(Sequence number: 8).

Amino acid sequence of the protein in which 15 amino acid residues at N terminal side of human derived liver type glucokinase are deleted, is shown.

(Sequence number: 9).

Base sequence of the primer used in PCR reaction in the following Example 6 is shown.

(Sequence number: 10).

Base sequence of the primer used in PCR reaction in the following Example 6 is shown.

Examples

Hereinafter, this invention will be described in concrete terms using Examples.

A process for purification of mutant type enzyme

In human glucokinase, there are liver type and pancreas type depending on the difference of promoter, and 15 residues at N terminal are different. In order to carry out crystallisation for the purpose of three-dimensional structure analysis, a mutant type enzyme which lacked a part or a whole of this region was made by the following process.

PCR reaction was carried out using cDNA of human liver type glucokinase cloned on pCR2.1 (made by INTROGEN Co.) and two kinds of primer sets, comprising

a combination of 5'-gtcacaaggagccagaagcttatggccttgactctggtag-3' (sequence number 6) and

5'-gaageeccaegacattgtteettetge-3 (sequence number 7), and

a combination of 5'-ccaggccagacagccaagcttatggtagagcagatcc-3' (sequence number 9) and

5'-gaageceacgacattgtteettetge 3' (sequence number 10).

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The Hind III, Cla I fragment of the obtained PCR product was substituted with Hind III-Cla I region of

liver type GK cloned at Hind III, Eco RI site of pFLAG/CTC vector (Eastman Kodak), and thereby

cDNAs encoding mutant type GK ($\Delta 1$ -11) which lacked 1-11 residues of liver type GK and mutant type

GK (Δ1-15) which lacked 1-15 residues were obtained. The sequence of the obtained DNA was confirmed,

and thereafter, these vectors were made as expression vectors, and Escherichia coli DH alpha strain

(made by Takara Shuzo company) was transformed.

Transformant was cultured in LB medium at 37°C till the absorption at 600 nm became 0.8, and

thereafter, isopropyl-1-thio-beta-D-galactoside (made by Wako Pure Chemicals Co.) was added so as to

become the final concentration of 0.4 mM, and the protein production was induced at 25°C for 16 hours.

Cultured Escherichia coli was collected using centrifuge, and it was suspended in a buffer containing the

following components (50 mM potassium phosphate (Potassium Phosphate) pH 7.5, 50 mM NaCl, 2

mM DTT, 0.5 mM Pefabloc SC (made by Kanto Chemicals Company), a proteinase inhibitor mixture

(made by Roche Co.)).

Collected Escherichia coli was pulverised by ultrasonic pulverisation method, and soluble fraction was

dialysed against aforesaid buffer, and thereafter, it was purified using HiTrapQ column (made by

Amersham Corp.). The GK fraction eluted from HiTrapQ column by potassium chloride gradient was

diluted to a salt concentration of 50 mM by dilution.

The diluted GK fraction was purified by Glucosamin Sepharose column produced by a process

demonstrated in the paper (Preparative Biochemistry, 20(2), 163-178 (1990)). The GK fraction was

adsorbed onto Glucosamin Sepharose column, and impurity was eliminated with 100 mM sodium chloride,

and thereafter, it was eluted by glucose of 1 M.

The eluted GK fraction was refined by MonoQ10/10 column. The GK fraction eluted from the

MonoQ10/10 column (made by Amersham Corp.) by sodium chloride gradient was purified by Superdex

200 column (made by Amersham Corp.) using 50 mM Tris-Cl pH 7.2, 50 mM NaCl buffer as mobile

layer.

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Crystallisation process

Crystal of mutant type GK [$\Delta 1$ -11] / glucose / compound complex

The crystal of mutant type GK ($\Delta 1$ -11) / glucose / compound complex was obtained using a technique of the following vapor diffusion. Moreover, mutant type GK ($\Delta 1$ -11) denotes a glucokinase containing amino acid sequence represented by Sequence Number 5.

In other words, mutant type GK purified to a high purity was concentrated, and finally a solution of mutant type GK of about 10 mg/ml (25 mM Tris-Cl, 50 mM NaCl, 5 mM TCEP) was formed. Thereto were added glucose of final concentration 20 mM and following compound 1 (compound of formula IIIa) which activates GK of final concentration 0.3 mM, and this was used for crystallisation. To protein solution 1-5 µl was added as crystallisation solution, an equal quantity of 28-30 % PEG 1500 and 0.1 M Hepes-NaOH (pH 6.6), and this solution formed by admixing was placed in a closed container containing 0.5-1 ml of crystallisation solution as that both solutions did not form contact, and the container was left to stand at 20°C. After standing for about 3 days - 1 months, crystals with maximum size of about 0.4 mm x 0.4 mm x 0.7 mm was obtained in the sample solution (Example 1).

Furthermore, the crystals obtained by aforesaid method were immersed for about 3-7 days in 28-80 % PEG 1500, 0.1 M HePes-NaOH (pH 6.6) solution so that the following compound 2 (compound represented by formula IIIb) was contained in a concentration of 0.3 mM, and thereby a complex crystals of the following compound 2 and aforesaid mutant type GK were obtained.

Compound 1

Compound 2

(IIIa)

Moreover, crystallisation was carried out in the same way as in Example 1 except that compound 3 (compound represented by formula IIIc) was used in stead of aforesaid compound 1, and as a result, crystals were respectively obtained in the same way as in Example 1 (Example 3).

Compound 3

$$0 = \stackrel{\mathsf{CH}_3}{=} 0 \qquad 0 \qquad \stackrel{\mathsf{CH}_3}{=} CH_3 \qquad (IIIc)$$

The obtained crystals were immersed into a crystallisation solution added with 10 % glycerol, thereafter it was rapidly frozen in liquid nitrogen. The X-ray diffraction data of the frozen crystal was collected in 100 K nitrogen gas stream by oscillation method at BL6B of synchrotron institution KEK-PF. From the obtained diffraction pattern, diffraction intensity was numerised using DENZO/SCALEPACK (made by HKL Co.), and crystal structure factor was determined. At this step, the crystal was found to be hexagonal system and had a space group of $P6_522$ or $P6_122$, and crystalline unit lattice was a = b = 79.9 angstrom, c = 322.2 angstrom, alpha = beta = 90° , gamma = 120° .

Using the obtained structure factor and three-dimensional structural coordinates of Human hexokinase type 1, the structure was analysed by molecular replacement method. Data with the resolution of 8 angstrom to 4 angstrom was used for the calculation, and it was performed by Amore program of CCP4 (Council for the Central laboratory of the Research Councils). The R factor of structure obtained by calculation was 53.7 %, and it was found that the space group of the crystal was P6₅22 and a single molecule of mutant type GK was contained in asymmetrical unit. Electron density map was obtained

from this structure and structure factor, and the structure of mutant type glucokinase was determined using a program O (made by Dat-ONO Company).

Thereafter, refinement of the position of amino acid was carried out using CNX (Accelrys Inc.) and identification of amino acid residue was carried out using program O. This operation was repeated, and the structural coordinate of 448 amino acid residues from threonine 14 of the mutant type glucokinase to cysteine 461, 1 molecule of glucose molecule, 1 molecule of compound A, 1 sodium ion and 149 water molecules were identified, and the structural coordinates were determined. The R factor which is used as index of accuracy of finally determined structure was R = 23.2 % with respect to the data of resolution from 30 angstrom to 2.3 angstrom, and the R factor (Rfree) with respect to the data which was not used for the calculation in the refinement step of the structure was 27.4 %. There was no amino acid residue having the unacceptable structure by confirmation with Ramachandran plot.

The structure of the determined mutant type glucokinase was similar to the structure of the hexokinase which was isozyme, but the structure of the binding site of compound 1 (compound of formula IIIa) which activates glucokinase was different. This structural difference could not be expected with the ability of current computational chemistry and it became clear for the fist time by this structural analysis that this site was the binding site of activator and its detailed stereostructure. Figure 1a is ribbon diagram showing three-dimensional structure of the glucokinase elucidated here. As shown in Figure 1a, the newly found activator binding site was located between large domain and small domain, and it was about 20 angstrom away from the active center wherein glucokinase bonded with the substrate, glucose. The amino acid residue of glucokinase constituting the activator binding site was as follows. Tyrosine 61 - serine 69, glutamic acid 96 - glutamine 98, isoleucine 159, methionine 210 - tyrosine 215, histidine 218 - glutamic acid 221, methionine 235, arginine 250, leucine 451 - lysine 459.

Moreover, the binding scheme of compound 1 (compound of formula IIIa) with respect to this binding site is shown in Figure 2 and the structure of binding site of glucokinase is shown in Figure 3. The thiazole ring formed van der Waals contact with each amino acid side chain molecule of valine 62, valine 452, valine 455, and moreover the nitrogen atom on thiazole ring was hydrogen bonded with nitrogen atom of main chain of arginine 63. The nitrogen atom of amide on compound 1 was hydrogen bonded with oxygen atom of main chain of arginine 63. Benzene ring part of compound 1 was formed van der

Waals contact with isoleucine 211, and the fluorine atom substituted to benzene ring formed van der Waals contacted with side chain of tyrosine 214. Aniline structure of compound 1 formed hydrogen bond with oxygen atom of side chain of tyrosine 215. Imidazole ring part bonded to the benzene ring via sulfur formed van der Waals contacted with amino acid side chain part of methionine 210, methionine 235, tyrosine 214. The serine 64-serine 69 part connecting the small domain and the large domain had a structure exposed to the solution, and compound 1 was bonded to the lower part of the arc-form structure formed by this part (Figure 3).

Example 4

Example of drug design

Using software UNITY (made by Tripos Company), pharmacophore of hydrogen bond acceptor and the hydrogen bond donor respectively generated from the main chain NH, CO of Arg 63, hydrophobic pharmacophore formed in the space corresponding to the phenyl group of aniline part of the ligand which formed the complex, and the protein surface formed on the basis of structure of the protein were used as search conditions, and Library compounds were screened, and the following compound 4 and compound 5 were obtained, and assay was carried out. As a result, activity of 780 % and 560 % was respectively observed. Wherein, the activity of 780 % denotes that the activity was enhanced upto 780 % by these compound when the activity of glucokinase of the control was 100 % (using glucose 2.5 M and ligand $10~\mu M$).

Compound 4

Activity: 780 %

Compound 5

Activity: 560 %

Example 5

Crystal of mutant type GK ($\Delta 1$ -15)

The crystal of simple substance of mutant type GK ($\Delta 1$ -15) (glucokinase containing amino acid sequence represented by Sequence Number 8) was obtained using the following vapor diffusion technique.

In other words, mutant type GK purified to a high purity was concentrated, and finally a solution of mutant type GK of about 10 mg/ml (25 mM Tris-Cl pH 7.2, 50 mM NaCl, 5 mM TCEP) was formed. To protein solution 1-5 µl was added an equal quantity of crystallisation solution (1.5-1.6 M ammonium sulfate, 50 mM NaCl, 0.1 M Bicine NaOH (pH 8.7)), and this solution formed by admixing was placed in a closed container containing 0.5-1 ml of crystallisation solution as that both solutions did not form contact, and the container was left to stand at 20°C. After standing for about 3 days - 1 months, crystals with maximum size of about 0.07 mm x 0.07 mm x 0.5 mm was obtained in the sample solution.

The obtained crystals were immersed into the crystallisation solution added with 20 % glycerol, and continuing it was frozen rapidly in liquid nitrogen. The X-ray diffraction data of the frozen crystal were collected by oscillation method in 100K nitrogen gas stream at BL32B2 of synchrotron institution Spring-8. From the obtained diffraction image, the diffraction intensity was numerised using Mosflm, and crystal structure factor was determined. At this step, it became clear that the crystal was hexagonal system and had space group of $P6_522$ or $P6_122$, and crystal unit lattice was a = b = 103.2 angstrom, c = 281.0 angstrom, alpha = beta = 90° , gamma = 120° .

Next, molecular replacement method was carried out using the obtained structure factor and structure was analyzed. As model of stereostructure, three-dimensional structural coordinates of each domain of glucokinase determined from the mutant type GK ($\Delta 1$ -11) / glucose / compound complex crystal was separately used. The calculation was performed by Amore program of CCP4 (Council for the Central laboratory of the Research Councils) using data of resolution of 8-4 angstrom. It was found that the space group of the crystal was P6₅22, and a single molecule of mutant type GK ($\Delta 1$ -15) was contained in the asymmetrical unit. Electron density map was obtained from this structure and structure factor, and the structure of mutant type GK ($\Delta 1$ -15) simple substance was determined using program O (made by Dat-ONO Company).

Next, refinement of position of amino acid was carried out using CNX (made by Molecular Simulation Company) and identification of amino acid residue was carried out using program O. This operation was carried out repeatedly, and the structure coordinate of 424 amino acid residues from asparagine 180 to cysteine 461 and from methionine 15 to histidine 156 of mutant type glucokinase, and 2 molecules of sulfate ions, 1 sodium ion and 7 water molecules were identified, and the structural coordinates were determined. The R factor which is used as index of accuracy of finally determined structure was R = 23.8 % with respect to data of resolution of 50-3.4 angstrom, and the R factor (Rfree) with respect to the data which was not used for the calculation in the refinement step of structure was 30.6 %. There was no amino acid residue having the unacceptable structure by confirmation with Ramachandran plot.

The ribbon diagram showing the structure of glucokinase ($\Delta 1$ -11) / glucose / compound 1 and the ribbon diagram showing the structure of glucokinase (Δ1-15) simple substance are respectively shown in Figure la and Figure 1b. Moreover, the figure on the right is a rotated figure of the figure on the left. In the structure of determined mutant type GK ($\Delta 1$ -15) simple substance, the structures of main parts of the large domain and the small domain were similar to the respective structures of glucokinase determined by mutant type GK (Δ1-11) / glucose / compound complex crystal, but relative position of two domains was greatly different. In mutant type GK (Δ1-15) simple substance structure, the main part of the small domain was rotated by about 99 degrees from position of small domain in mutant type GK ($\Delta 1-11$) / glucose / compound complex structure. Moreover, alpha 13 helix located at C terminal region of glucokinase which constituted the small domain in the mutant type GK (Δ1-11) / glucose / compound complex structure no longer constituted the small domain in the mutant type GK (Δ1-15) simple substance structure, and it was located at between two domains. Moreover, because both the activator binding site and binding site of substrate, glucose were present between two domains in the mutant type GK (Δ1-11) / glucose / compound complex structure, the structures of their sites were greatly changed in the newly determined structure. The amino acid residues that play an important role in enzyme activity did not form active site in the mutant type GK ($\Delta 1$ -15) simple substance structure, and the structure of mutant type GK (Δ1-15) simple substance analysed here was a structure of inactive state of glucokinase. Moreover, the activator binding site had completely disappeared in the structure of mutant type GK (\Delta1-15) simple substance. The structural change of glucokinase (rotation of domains about 99°) observed by the mutant type GK ($\Delta 1$ -11) / glucose / compound complex structure and the mutant type GK ($\Delta 1$ -15)

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simple substance structure was far greater compared with the previously known structural change of

hexokinase (rotation of domains about 12°), and it could not be expected with the ability of current

computational chemistry and it became clear from this structure analysis for the first time.

Moreover, in order to hinder the structural change to the inactive form mutant type GK ($\Delta 1$ -15) simple

substance structure, by designing a compound that binds to the compound binding site indicated by the

mutant type GK ($\Delta 1$ -11) / glucose / compound complex structure, it became clear that activator of

glucokinase could be designed.

Possible Applications in Industry

As described above, in accordance with this invention, crystal of the glucokinase protein which was

difficult to crystallise in the prior art was obtained. The three-dimensional structural coordinates

obtained by analysing this crystal structure can be suitably used in order to design compounds that bind to

glucokinase. Moreover, because the compounds designed in this way bind to glucokinase, they can be used

as therapeutic agent of disease involving the glucokinase activity (for example diabetes mellitus

therapeutic agent) as glucokinase activator or inhibitor.

Patent Claims

1. A glucokinase protein characterised in being used for crystallisation.

2. A protein in accordance with Claim 1 comprising amino acid sequence in accordance with Sequence

Number 5.

3. A crystal of protein comprising amino acid sequence in accordance with Sequence Number 5 or amino

acid sequence substantially the same amino acid sequence thereof.

4. A crystal in accordance with Claim 3, wherein the said protein is glucokinase protein.

5. A crystal in accordance with Claim 3 comprising crystals of protein containing amino acid sequence in

accordance with Sequence Number 5.

6. A crystal in accordance with Claim 3, wherein the lattice constant satisfies the following equations (1)-(4)

$$a = b = 79.9 + /-4 \text{ Å}$$
 (1)

$$c = 322.2 + / - 15 \text{ Å}$$
 (2)

$$alpha = beta = 90^{\circ}$$
 (3)

$$gamma = 120^{\circ} \tag{4}$$

- 7. A crystal in accordance with Claim 6, wherein the space group is P6₅22.
- 8. A crystal of protein specified by three-dimensional structure coordinates data in accordance with Table 1.
- 9. A crystal wherein in three-dimensional structure coordinates data changed in at least one data of three-dimensional structure coordinates data in accordance with Table 1, the mean square error between atoms of main chain of amino acid represented by three-dimensional structure coordinates data in accordance with Table 1 (C alpha atom) and C alpha atoms represented by the said changed three-dimensional structure coordinates data corresponding to aforesaid C alpha atoms is 0.6 Å or less.
- 10. A crystal in accordance with any of Claims 3-9, wherein the compound binding site is constructed by at least one of amino acid residues of tyrosine 61 serine 69, glutamic acid 96 glutamine 98, isoleucine 159, methionine 210 tyrosine 215, histidine 218 glutamic acid 221, methionine 235, arginine 250, leucine 451 lysine 459 in amino acid sequence shown in sequence Number 5.
- 11. A crystal including a complex of the protein comprising amino acid sequence in accordance with Sequence Number 5 or amino acid sequence substantially the same amino acid sequence thereof and a compound which can bind to the said protein.
- 12. A crystal in accordance with Claim 11, wherein aforesaid compound is represented by formula (1).

[wherein, R1 shows halogen atom, -S-(O)p-A, -S-(O)q-B or -O-B (wherein, p and q are the same or different and denote an integer of 0-2, A denotes C1-C6 alkyl group of optionally substituted straight chain, B denotes optionally substituted five-membered or six-membered ring aryl group or heteroaryl group, R2 denotes a hydrogen atom or halogen atom, and

denotes an optionally substituted monocyclic or bicyclic heteroaryl group having a nitrogen atom adjacent to the carbon atom bonded to amide group].

13. A crystal in accordance with Claim 12, wherein aforesaid compound is any of the compound represented by formula (IIIa)-(IIIc).

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$$0 = \stackrel{\mathsf{CH}_3}{=} 0 \qquad 0 \qquad \stackrel{\mathsf{S}}{=} 0 \qquad \mathsf{CH}_3 \qquad \mathsf{CH}_3$$

$$\mathsf{NH}_2 \qquad \mathsf{(IIIc)}$$

14. A protein in accordance with Claim 1 comprising amino acid sequence in accordance with Sequence Number 8.

15. A crystal of protein comprising amino acid sequence in accordance with Sequence Number 8 or amino acid sequence substantially the same amino acid sequence thereof.

16. A crystal in accordance with Claim 15, wherein the said protein is glucokinase protein.

17. A crystal in accordance with Claim 15 comprising crystals of protein containing amino acid sequence in accordance with Sequence Number 8.

18. A crystal in accordance with Claim 15, wherein the lattice constant satisfies the following equations

$$a = b = 103.2 + /-5 \text{ Å}$$

$$c = 281.0 + /- 7 \text{ Å}$$

$$alpha = beta = 90^{\circ}$$

gamma =
$$120^{\circ}$$

19. A crystal in accordance with Claim 18, wherein the space group is P6₅22.

20. A crystal of protein specified by three-dimensional structure coordinates data in accordance with Table 2.

21. A crystal wherein in three-dimensional structure coordinates data changed at least one data of three-dimensional structure coordinates data in accordance with Table 2, the mean square error between atoms of main chain of amino acid represented by three-dimensional structure coordinates data in accordance

with Table 2 (C alpha atom) and C alpha atoms represented by the said changed three-dimensional structure coordinates data corresponding to aforesaid C alpha atoms is 0.6 Å or less.

- 22. A process for the production of crystal containing a complex of protein and a compound that binds to the protein thereof, including
- a protein production step wherein a protein containing the amino acid sequence having deletion of 1-50 amino acid residues from either or both of N terminal and C terminal of the protein containing amino acid sequence in accordance with Sequence Number 2 is produced, and
- a protein reaction step wherein a compound that binds to the protein obtained in the said protein production step and the protein obtained in the said protein production step are reacted.
- 23. A process to produce crystal of the kind wherein a crystal of a protein is produced, characterised in that a protein including amino acid sequence in accordance with Sequence Number 5 or amino acid sequence substantially the same amino acid sequence thereof and having glucokinase activity and a compound which can bind to the said protein are used.
- 24. A process for the production of crystalline protein in accordance with Claim 23, wherein the compound which can bind to said protein is a compound represented by formula (1).

(1)

[wherein, R1 shows halogen atom, -S-(O)p-A, -S-(O)q-B or -O-B (wherein, p and q are the same or different and denote an integer of 0-2, A denotes C1-C6 alkyl group of optionally substituted straight chain, B denotes optionally substituted five-membered or six-membered ring aryl group or heteroaryl group, R2 denotes a hydrogen atom or halogen atom, and



denotes an optionally substituted monocyclic or bicyclic heteroaryl group containing nitrogen atom adjacent to the carbon atom bonded to amide group].

25. A process for the production of crystal in accordance with Claim 23 or 24 using co-crystallisation or soaking method

26. A drug design method of the kind wherein based on stereostructural information of a protein, the structure of compound that binds to said protein is designed, characterised in that the stereostructure information of said protein is the information obtained by analysing crystal in accordance with any of Claims 3-13 or 15-21.

27. A drug design method in accordance with Claim 26 characterised in that

a binding site deduction step wherein the compound binding site of said protein is deduced based on aforesaid stereostructure information, and

a selection step wherein a compound compatible to the compound binding site deduced in aforesaid binding site deduction step is selected from compound library, are included.

28. A drug design method in accordance with Claim 26 characterised in that

a binding site deduction step wherein the compound binding site of said protein is deduced based on aforesaid stereostructure information, and

a compound structure assembly step wherein the structure of compound compatible to compound binding site deduced in aforesaid binding site deduction step is constructed, are included.

29. A drug design method in accordance with Claim 26 characterised in that

a binding site deduction step wherein the compound binding site of said protein is deduced based on

aforesaid stereostructure information, and

a design step wherein the structure of compound is designed by visual observation so that the compound

binding site deduced in aforesaid binding site deduction step and a compound compatible to said

compound binding site interact,

are included.

30. A drug design method in accordance with any of Claims 26-29, wherein aforesaid compound binding

site is constituted by at least one of amino acid residue of tyrosine 61 - serine 69, glutamic acid 96 -

glutamine 98, isoleucine 159, methionine 210 - tyrosine 215, histidine 218 - glutamic acid 221,

methionine 235, arginine 250, leucine 451 - lysine 459 in amino acid sequence shown in sequence

Number 5.

31. A drug design method in accordance with any of Claims 26-30 further including a step to measure

physiological activity of the candidate compound predicted to be compatible to aforesaid compound

binding site.

32. A drug design method in accordance with any of Claims 26-30 further including a binding

determination step wherein the candidate compound predicted to be compatible to aforesaid compound

binding site and a protein including amino acid sequence in accordance with and Sequence Number 5 or

amino acid sequence which is substantially the same amino acid sequence thereof are contacted, and

whether the candidate compound binds to the said protein or not is assessed.

33. A process for the production of compound array including the compound group selected by drug

design method in accordance with any of Claims 26-30 is combined as compound array.

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